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OXFORD MEDICAL PUBLICATIONS

A
SYSTEM OF SYPHILIS

IN FIVE VOLUMES

EDITED BY
D'ARCY POWER, M.B. Oxon., F.R.C.S.
AND
J. KEOGH MURPHY, M.C. Cantab., F.R.C.S.

WITH AN INTRODUCTION
BY
The late Sir JONATHAN HUTCHINSON, F.R.S.

VOL. I.

INTRODUCTION	Sir JONATHAN HUTCHINSON, F.R.S.
HISTORY	IWAN BLOCH, M.D.
MICROBIOLOGY	Professor ELIE METCHNIKOFF
GENERAL PATHOLOGY .	F. W. ANDREWES, M.D. Oxon., F.R.C.P.
EARLY MANIFESTATIONS, MALE.	The late Colonel F. J. LAMBKIN, R.A.M.C.
EARLY MANIFESTATIONS, FEMALE	A. SHILLITOE, F.R.C.S.
CONGENITAL SYPHILIS .	G. F. STILL, M.D., F.R.C.P.
RECENT MICROBIOLOGY .	Major L. W. HARRISON, R.A.M.C.

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TO THE MEMORY OF

FRITZ SCHAUDINN (1871–1906)

AND BY KIND PERMISSION TO

ALFRED FOURNIER
ERICH HOFFMANN
AND THE LATE
SIR JONATHAN HUTCHINSON, F.R.S.

IN RECOGNITION OF THE VALUABLE WORK

DONE BY EACH TOWARDS THE

PREVENTION AND CURE

OF

SYPHILIS

EDITORIAL PREFACE

Syphilis has been considered a special disease for too long a time. It has continued to be called 'specific' when less was known of its nature than about many other disorders, and it has been dealt with as though it differed in its course from all other affections. The advance in medicine, due to improvements in pathology, has enabled syphilis to be classed with the infective diseases, and experiment has discovered the micro-organism which causes it.

The time has come, therefore, when syphilis can be discussed and its signs, symptoms, and treatment can be described from the standpoint of modern medicine and surgery. To this end the Editors have obtained the assistance of writers who have made their reputation in the general fields of medicine, surgery, ophthalmology, gynaecology, and public health, as well as of others who have had unrivalled opportunities for studying the early stages of venereal diseases. The individual articles have thus gained in breadth of view without losing in depth of knowledge.

The aspects of syphilis are protean, and its results are seen in every tissue of the body. Each writer finds more than enough to tell about its effects in his own branch of practice; and whilst each has been allowed a free hand, an attempt has been made to harmonize the general views expressed. Some conflict of opinion is both necessary and desirable: necessary, because no two persons draw the same conclusions from similar sets of facts; desirable, because a difference of opinion often stimulates thought and leads to further advance.

It will be found, too, that there is some repetition, especially in regard to the treatment of syphilis. Such repetition was thought to be a good feature, since the prevention and cure of the disease are of the first importance to the community, and methods which can be carried out in the public services and in our great charities are not always suitable or desirable in private practice.

Some attempt, too, has been made to deal exhaustively with the subject of Syphilis by including articles upon ‘ Syphilis and Life Insurance ’; ‘ Syphilis in its Medico-Legal Aspects ’; and ‘ The Mental Affections of Syphilis ’, upon all of which too little stress has been laid in the past.

The historical side of the question has been dealt with most ably by Dr. Iwan Bloch, who has devoted much time and work to elucidate the source of the European pandemic at the end of the fifteenth century.

The late Sir Jonathan Hutchinson summed up in his introduction the mature conclusions of a lifetime devoted to a study of syphilis. His words will be read with the respect due to the father of modern syphilology in England, and every one interested in the subject will rejoice to think that he survived to see syphilis founded on a sure basis of experiment, and freed for ever from the charlatanism which has long surrounded it. The existence of a book containing an introduction by Sir Jonathan Hutchinson and an article by Prof. Metchnikoff shows how uninterrupted has been the progress of the scientific knowledge of syphilis during the last fifty years.

Finally, the Editors cannot end these few forewords without paying a tribute to the generosity with which the Publishers of the work have met the requests of the writers that their articles should be adequately illustrated by the most modern methods familiar to art. For the direct colour photographs used for the first time in this work to illustrate clinical conditions they are much indebted to Dr. Arnold Moritz and to Mr. Tubbs. They desire also to record their appreciation of the great kindness of Lieut.-Col. Sir W. B. Leishman in allowing the use of his very beautiful specimens.

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VOL. I

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INTRODUCTION

The proposal of which the present volume is in part the accomplishment has been made at a singularly appropriate time. The discovery made by Schaudinn, and subsequently developed by an army of enthusiastic workers on his lines, promises to throw much new light upon the many problems which the study of syphilis presents. It was a worthy and well-judged design on the part of the present Editors to prepare a work in which those problems should be discussed in full detail.

Impressed by this fact I accepted with pleasure the compliment which was paid to my own seniority in the request that I would write a short prefatory chapter to the work.

In attempting to carry out my undertaking, I have found it exceedingly difficult to restrict myself to the space at my disposal. The subject is very large and the topics very varied. It has seemed that more, that will be useful to the reader in the way of suggestion, can be put into a small space in the form of detached paragraphs than by attempting a consecutive essay. It is in this condition that the following pages must be accepted. They are intended chiefly to suggest lines of profitable thought and future inquiry.

It was said long ago of syphilis, that it constitutes in itself an epitome of pathology. This statement finds at the present time increasingly abundant illustration. There is scarcely a malady which has received a name which may not be simulated by it, and still fewer which it may not modify. The explanation of this is no doubt to be found in the fact that the stages of the syphilitic fever are so protracted that all the tissues of the body come under its prolonged influence, and that it thus enters into partnership with all the pre-existing proclivities of the individual. To these varying proclivities, taken in conjunction with the measures of treatment adopted, it is in the main that we must attribute the very various aspects which its manifestations assume. Although the discovery of the spirochaete is new, the conclusions to which it points are not so. They have been accepted and acted upon very definitely ever since the time when syphilis was first claimed as a slow-staged exanthematic fever resulting from a specific *contagium animatum.*

Schaudinn's discovery, however, has added most importantly to the precision of our knowledge, and has placed what was formerly only matter of assured inference upon the secure basis of demonstrated fact. Side by side with it must be placed the almost simultaneous demonstration that it is possible to communicate this fever to certain animals nearly allied to man. Thus a field for experimental study has been opened which was not accessible to our predecessors, and from the working of which very valuable results may be confidently expected. It is, however, desirable to extend a caution to those who engage in this line of inquiry, that their inferences must not be too hastily accepted. There is danger that the outcomes of purposeful experiments may be allowed to seem much more conclusive than they really are.

Thus John Hunter, acting on his precept, 'Don't think, try,' convinced himself that gonorrhoea and syphilis were caused by the same poison; and his conclusion, based as it was upon an experiment, was allowed to influence professional opinion, very injuriously, during a long series of years.

Unless much caution be exercised both as regards experiments on apes and monkeys and the microscopic demonstration of the parasite, it may be reasonably feared that the knowledge of syphilis for practical purposes may be hindered rather than advanced by the recent brilliant discoveries. It might have been safer to continue to base our conclusions on careful observations of what actually occurs in the human subject. For those who can see and are willing to observe, record, and compare, many valuable experiments are brought under our notice in which our hands have taken no part. The discovery of the bacillus of leprosy may not improbably have had the lamentable result of retarding for a quarter of a century that kind of knowledge of the disease upon which practical measures could be safely based. It was allowed to re-establish the old and outworn doctrine of contagion which is only in the present day again fading from the creed of the profession. We need not fear that any hasty inference of this kind will lead us to regret Schaudinn's discovery, but there are possible pitfalls.

For the present there are no indications that any important modifications of doctrine or practice will follow. The results of experiment and histological research can of course never really conflict with those of clinical study, but it will be a misfortune if the brilliancy of the former is allowed even for a time, to throw the latter into shade or in any degree to damp the zeal of those who take what may perhaps after all prove to be the safest road.

One of the important lessons which the investigation of syphilitic facts has offered to the student of the laws of pathogenesis in general, is the demonstration of the possibility of absolute and very prolonged latency of forces destined ultimately to manifest conspicuous activity. The facts alluded to occur both in the acquired and inherited forms of the disease. A patient who after an apparent cure of the disease has enjoyed many years of uninterruptedly good health, and who has possibly been the parent of a long series of healthy children, may suddenly become the subject of nodes or gummata concerning the nature of which there can be no doubt. Even more remarkable are the facts which have been established in reference to the peculiar form of keratitis which is now acknowledged to be a direct result of inherited taint. Not only may the period of adolescence have passed but that of middle age may have been reached before the patient experiences any indication of corneal disturbance. Children may have been born, the health may have been excellent, and there may still be entire absence of all other indications of the malady when the two eyes, almost simultaneously, become engaged in an acute and severe attack of inflammation, of a quite characteristic type. Nor is the wonder diminished when it is added that these long-delayed attacks are, like those of the earlier stages, destined to subside spontaneously and with the almost complete certainty that there will be no recurrence. The inference is suggested that there must have existed all the time in the corneal tissues, some material capable of causing irritation, but which a single attack of inflammation sufficed entirely to exhaust. It is difficult perhaps to suggest any exact parallel from the domain of general pathology.

It may perhaps at first sight be thought that these prolonged periods of possible latency lend some plausibility to the suggestion that it is possible for syphilis to be inherited in the third generation. A little consideration may, however, suffice to show that they do not by any means go that length. As regards this possibility we can scarcely hope that unanimity of opinion will ever be attained. Those who see nothing very improbable in the occurrence will easily give credence to the statements of their patients and the records of their confrères, whilst those who think that, if possible, it would be frequent, and in whose experience every supposed example has broken down under investigation, will remain incredulous.

The extreme rarity of any event in such a disease as syphilis must not, however, be allowed to make us believe that it is impossible. It may, however, quite legitimately justify a refusal to permit such supposed facts to exercise any material influence on our conduct. Counsels of perfection are by no means always wise ones. The conditions of social life render it necessary that certain minute risks must now and then be encountered by individuals in the pursuit of the general good. Thus, although we may possibly be compelled to admit that it is possible for a man to communicate syphilis to his wife or child although an interval of more than two years may have passed before marriage, the extreme infrequency of the occurrence may fully justify us in declining wholly to forbid such marriages and make us content with enforcing prolonged treatment. So also with transmission to the third generation. It would be absurd to deny its possibility as a matter of theory, but the evidence as to its rarity so nearly approaches the conclusion that it never occurs, that we may safely ignore it.

The rehabilitation of *Mercury* in professional esteem, which has followed on what has been witnessed in the small-dose treatment of syphilis, must surely be credited as a very important advance in general therapeutics. Now that we know how to use the drug rationally we are no longer afraid of it, and are able by confident statements to overcome the prejudices of our patients. The future will doubtless witness much further progress in these directions; for the beneficial influence of minute doses of mercury is far from being restricted to the case of syphilis and its results. It may be combined with tonics or guarded by opiates, and when thus judiciously adapted will agree with almost every one and may be continued for almost any length of time. The nearly invariable testimony of those who have taken long courses for the treatment of syphilis is, that they enjoy better health than ever before. The secret is to keep the dose small enough and to continue it long enough. It may be given in this manner in all climates to all races and at all ages, and with little or no interruption of the patient's ordinary mode of life. My experience in this matter has been such that I may confess to feeling much jealousy of some modern modes of administration from a fear that they may prejudice the reputation of an invaluable drug.

As regards the prevention of tertiary phenomena—by far the most important aim in the treatment of syphilis,—whilst the general conclusions are overwhelmingly in favour of mercury as compared with doing nothing, it may be reasonably doubted whether it is possible to construct satisfactory statistics as to the different methods of administration. Several quite distinct features in the treatment are concerned and it may lead to error if only one or two are attended to. Cases are not fairly comparable unless the mercury was begun at the same stage of the disease and continued over the same periods of time. Above all it is important that the date of beginning should have been the same, for it may be regarded as probable that the later phenomena are for the most part local recrudescences of those which have gone before. Thus the '*abortive treatment*' which begins before the development of the secondary symptoms and aims at their prevention is far more likely to obviate tertiaries than any measures, however vigorous and however long continued, which have been delayed to a later stage.

It may be plausibly conjectured that the measures employed by our forefathers who gave mercury indiscriminately for all venereal sores, who began at once and pushed it to full saturation of the patient's tissues, was, although undesignedly so, in reality *abortive*, and very efficiently so. It was possibly, although not without serious drawbacks, more truly abortive than any which we now, more timorously, venture on. It may have killed the spirochaete before it had time to breed and to establish foci. Only a short period has elapsed since all authorities insisted that it was not justifiable to begin mercury until the appearance of secondary symptoms had established the diagnosis. Nor had any one any conception that it was practicable to entirely prevent the occurrence of those symptoms by the anticipatory use of this priceless specific. That fact has now been abundantly demonstrated, and the precept that treatment should be commenced as soon as ever the diagnosis is established is now generally accepted, with the most beneficial results. It may indeed be acknowledged as by far the most important step in the therapeutics of syphilis which has been taken during the last century; for the prevention of secondaries probably means the prevention of tertiaries also. If, as seems not improbable, the discovery of the spirochaete should place at our disposal a trustworthy means of recognizing syphilitic chancres in their earliest stages it will be a gain for which we may well be thankful.

The nature of the relationship which exists between certain maladies which have been recognized in distant regions, and some of them in distant ages, and what we now know as European syphilis, is sure to continue to cause discussion in the future. In Ceylon we now have 'parangi' ('the foreigner's disease'); in Fiji 'thoka', an indigenous malady; in the West Indies and on the West African coast 'yaws'; whilst in Scotland and Ireland there were formerly little epidemics of what was called 'sibbens' and 'button scurvy'. In quite recent times the Dublin surgeons recognized what they called *Morula* and considered to be distinct from syphilis. All these have it in common that the skin eruption is a fungating one (framboesiform), and by most modern writers they are all now placed together under the meaningless and ugly name of 'yaws'. Meanwhile no one can define that term or give to it any descriptive limitations. By one authority it was distinguished from syphilis by the supposed absence of any primary sore, and by another by the absence of throat affection from the rôle of secondaries. Both of these have been proved to be mistakes, and it is now recognized that yaws, like syphilis, has its chancre and bubo and its symmetrical sores on the tonsils, and that it observes in its development the same stages as syphilis does, and may be followed by the same tertiary affections of the skin and bones. The chancre had been overlooked because it is usually non-venereal and not located on the genitals. A few years ago the position of those who asserted that yaws and syphilis were not specifically distinct seemed assured, and those who were engaged in the treatment of yaws were recording in triumph the good results of the small-dose method. The first outcome of Schaudinn's discovery seemed to substantiate these conclusions, for the parasite was found in Cingalese cases of 'parangi'. Further research has, however, been held to throw doubt upon the identity of the two diseases. Minute differences have been detected between the two spirochaetes, and experiments have seemed to show that the one disease is not absolutely protective against the other. It is possible, however, that these apparent differences may prove to be more apparent than real. It may perhaps prove to be the fact that the spirochaete bred in different climates and in different races is capable of some modifications. These modifications may no more constitute specific characters than do the horns of a Scotch sheep or the hornless dusky face of a well-bred Southdown. All our domestic sheep are unquestionably of one species, and in spite of their very conspicuous differences and the fact that they usually breed true, they may be crossed and are prone to revert.

Meantime the advocates of specific identity have the facts that in countries where syphilis alone is supposed to prevail, every now and then an isolated example of yaws is seen; that whenever an Englishman contracts yaws abroad he comes home with syphilis; that in yaws districts typical examples of the frambоesial eruption often follow hard chancres on the genitals. Further they may allege that where the two occur in the same community it is generally observed that the one appears to exclude the other. Now that it is generally accepted that syphilis was brought into Europe from the West Indies,* it is of interest to call to mind that the disease chiefly prevalent in those islands presents the features of 'yaws' and is called by that name. This statement is true also of the West Coast of Africa, another possible place of origin of syphilis.†

For the student of pharmacology syphilis has many important lessons. The marvel which we witness in the certain and speedy disappearance under the influence of mercury of a large sclerosis as hard as cartilage, is more than equalled by the melting away of a big tumour-gumma under that of iodide of potassium.‡ In each instance, if the drug is continued until all traces of the lesion are removed there is not as a rule any tendency to recurrence or at any rate not until after a long period of immunity. We may assume that in the early stages of syphilis the first and most important effect of mercury is to destroy the parasite, but it is more difficult to explain its action upon later lesions, and exceedingly difficult to assign that of the iodides in the case of large gummata.

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* To some of us who have for long insisted that no other conclusion was possible it is satisfactory to have the support of an authority such as Iwan Bloch. 'All available statements and facts point to the last decade of the fifteenth century—particularly the years 1493-1500—as the time when syphilis first appeared in the Old World. There is not a particle of evidence to show that the disease existed in Europe before that time.' This long and hotly debated question may perhaps now be considered as finally decided.

† Those interested in the study of 'yaws' may do well to examine a considerable series of portraits, &c., collected in the museum of the London Polyclinic, or to refer to the XIVth Fasciculus of the New Sydenham Society's Atlas. The latter concerns only the parangi of Ceylon.

‡ In a case recorded in my Archives, tumours in the liver, so large that they were easily visible as the patient rested on his back, were absorbed in the course of a few weeks and never recurred.

Can the foetus be infected with syphilis by its male parent only? This question has in the past been answered with much emphasis in opposite senses by good authorities. Of late the almost universal conclusion has been in the affirmative, but the discovery of the spirochaete and the observation that its size precludes the possibility of its entering a spermatozoon, has been recently held by some to put an end to all controversy. In the present state of our knowledge of the life-phases of the parasite we may, however, reasonably suspend our judgement, more especially when remembering that the clinical evidence is overwhelming in proof that a tainted child may be born to a mother who has herself never shown any suspicious symptoms.

On the supposition that the male parent cannot infect the foetus, in what way does the mother receive the contagion in the very numerous cases in which she apparently remains in good health?

Can any general laws be established as regards what is called 'the latency of syphilis', and can limits be assigned to its possible duration? Under what conditions does the spirochaete or its representative exist during latency? These questions must be considered separately in reference to the primary, secondary, and tertiary stages.

In the keratitis of inherited syphilis there is seldom or never any simultaneous affection of the skin, mucous membranes, or viscera, but very frequently of certain fibrous structures such as those of joints, the periosteum, &c. Is there in this fact any clue to the elucidation of our problems?

Can any explanation be given of the preponderating liability of the female sex to the late results of inherited taint?

What is the element or influence which is superadded to the spirochaete in cases in which primary syphilitic sores ulcerate or become phagedaenic or gangrenous ?

In explanation of the differences in the symptoms presented in different cases of syphilis in all its forms and all stages, two groups of causative influences may be plausibly suggested. First, the parasite may acquire in connexion with the race or constitutional state of its host, modifications which it may retain and perhaps accentuate in transference, but which by no means constitute specificity and from which reversion is always possible. A second and probably by very far the more important influence is the idiosyncrasy of the person by whom the poison is received. Thus the parasite serves to detect and reveal personal peculiarities of structure giving tendency to peculiarity in morbid manifestation.

The primary and universal effect of the presence of the syphilitic parasite may be assumed to be vascular dilatation and the other conditions which characterize common inflammation, with tendency to hypertrophic growth. The special peculiarities of each case will depend upon the structure or tissue most vulnerable and chiefly attacked.

It is an open question whether the tissue in which the virus is first implanted is of any importance as modifying the development of the disease. Does the virus subsequently travel in any sort of association with germinal matter derived from the site of infection ? It has been supposed that chancres affecting the nail are prone to produce general onychitis, and that sores on the skin will be followed by more severe eruptions than those on mucous membranes. Nothing, however, has been proved or even made probable in these directions.

If the patient who contracts syphilis be already the subject of tuberculosis, will the course of his syphilis receive any modifications ? Can there be any sort of partnership between the virus of syphilis and the bacillus of tubercle ?

Do peculiarities of race stamp any special features on syphilitic manifestations ? I have myself studied syphilis chiefly in London, but in representatives of the most various nations and races. I have also procured some opportunities of observation in South Africa, in Ceylon, and in India. I have formed an impression that in natives of the dark races there is a far greater tendency to framboesiform eruptions—that is, to papillary hypertrophy—and somewhat less to ulcerative inflammation than in Europeans. A Cingalese, temporarily resident in London, there contracted syphilis from an English woman, but the eruption which followed might have been considered characteristic of 'parangi'.

It is surely an important proposition that the syphilitic poison can cause not only inflammatory swelling but actual growth. This is best illustrated in the production of fimbriated papillomata on the surface of the tongue, but it occurs also in condylomata and all framboesial eruptions. We may suitably remember that in many plants the presence of a parasitic fungus stimulates growth.

In the secondary stage of syphilis the whole arterial and capillary system is affected. In many instances it probably receives some permanent damage. Hence probably the liability to degenerative changes at remote periods and under the influence of local strain.

In the attempt to assimilate tabes and general paralysis it is possible to go much further than is consistent with clinical convenience. Although they often coexist they are in many cases very distinct. Ataxy is probably, throughout, degenerative and requires rest and feeding, whilst general paralysis has its inflammatory stages and requires the continuous use of mercury.

The influence of syphilis in the production of recurring herpetic eruptions is worthy of careful study. These are unquestionably located by nerves and are often most definitely unilateral. They occur not only on the genitals but in the mouth and throat, where they may be very troublesome and are less transitory than other forms of herpes. They are often diagnosed as 'mucous patches', but if carefully observed they will be seen to be distinctly unilateral and grouped. They require for their prevention quinine or arsenic, and not mercury.

It might save innumerable blunders if we could entirely disuse the term 'soft sore' or *ulcus molle.* For it should be substituted that of 'non-indurated', and it should be understood to apply only to the date of the observation. As at present used, 'soft' does not mean anything more than absence of specific hardness. The venereal ulcers in which this one negative feature is recognized vary exceedingly amongst themselves in all others. Some are single, others are multiple, some are punched out, others elevated, and the majority present no characteristic features. It is impossible to predicate of any sore in which hardness is absent that it will not lead to syphilis, and to use the term 'soft' as implying such forecast, is, but too often, to mislead and disappoint the patient and imperil the reputation of the surgeon.

The commendation which arsenic has recently obtained in reference to syphilis, depends, we may suspect, not so much upon its influence on the parasite as upon its well-known power in controlling most forms of chronic dermatitis and especially upon its almost specific power in regard to bullous eruptions (pemphigus) and herpes. If this is true, the simultaneous use of mercury ought never to be omitted.

Many years ago I gave an address with the title, 'Syphilis as an Imitator.' It would have been better, 'Syphilis as a detector or as a revealer.' What is effected during the syphilitic fever and after it, is the bringing into activity somewhat tumultuously of the latent proclivities of the individual attacked. In the address quoted, liberty was taken to compare syphilis to the Evil One, and to quote the words of a popular theologian, 'He can mar, but he cannot make, for he is not antagonist deity'. Thus syphilis creates nothing new, but modifies every tendency that is already existent. Is its victim one in whom psoriasis might have easily occurred, it will bring out a hasty, crude form of that type of eruption; and the same is true of pemphigus, lichen, and most others. A fact in confirmation of this suggestion is to be found in the circumstance that arsenic, the specific for pemphigus diutinus, is necessary to the cure of syphilitic pemphigus.

Having repeatedly used the expression 'small dose method', it may be convenient to explain precisely its meaning. I apply it to the use of the grey powder pill, and it is understood that it is to be continued regularly, without any intermission, over a period of from one to two years. The pill contains from one to two grains of the grey powder, with from one to three of Dover's powder, and is given from three to six times a day. It is best to begin with one grain of the mercurial and two of the opiate, and not oftener than three times a day, and after food. Meanwhile all soups, green vegetables, fruit, and malt liquors are peremptorily forbidden, and an alum mouth-wash is employed. It is essential to avoid the occurrence of diarrhoea; of ptyalism there is but little fear. As soon as it has been ascertained what the patient can bear, the pill may be modified and the dose of mercurial increased. This is best done by increasing the frequency of the dose. If desirable quinine or nux vomica may be added. The quantity of mercury should be sufficient to cause the prompt and complete disappearance of symptoms. Neglect to regulate the diet often causes disappointment by permitting diarrhoea.

The facts as regards what have been termed 'Recurred chancres' are well worthy of more detailed examination and criticism. These indurations belong undoubtedly to the tertiary period. They illustrate forcibly the connexion which exists between tertiary or late phenomena and the previous occurrence of changes on the same spot in the primary or secondary stage. They develop on exactly the site of the first chancre, and resemble it in all features, being often as hard as cartilage. There may, however, have been an interval of perfect soundness, extending over several, or many years. They do not appear to be contagious and they are not as a rule accompanied by other symptoms and never by buboes. They yield slowly to treatment, far more slowly than primary sores. They may recur more than once. What relation does the spirochaete bear to these indurations? I know of one instance only in which it has been searched for, and in this we were unable to find it.

Amongst the most interesting of the imitations which syphilitic lesions accomplish are the simulations, by gummata, of malignant new growths. It is quite certain that these may develop rapidly and in persons in whom they are solitary phenomena. They may attain a large size and often lead to erroneous diagnosis. The suggestion that they are purely local is supported by the fact that even the largest usually melt away quickly under treatment, and that once absorbed they but rarely return.

The rôle of phenomena which constitute the primary and secondary stages of syphilis may often be incomplete. There may have been no chancre at all. Again, the chancre may never have been in any way characteristic, the glands may have wholly escaped, and the eruption, or the throat, one or both may be wholly absent. Finally, it must be admitted that *all* the symptoms usually displayed in the primary and early secondary stages may have been absent, and yet constitutional syphilis may have been acquired. It is difficult, indeed impossible, to assign limits to these suppressions, and their full recognition is a matter of the utmost importance in practice.

The omission of anything approaching to specific induration, in sores which yet prove infective, is a matter of everyday occurrence. A good half of those who come under my observation in the secondary or tertiary stage tell me that their original sore was confidently pronounced to be ‘ soft ’.

The entire omission of everything which could be deemed worthy the name of chancre or ulcer is also frequent. The patient may admit that he has had ‘ a little redness or abrasion which was well in a few days', but is sure that 'there was nothing more'. In other cases no history even of an abrasion may be obtainable. This may occur in cases in which the site of inoculation was recognized, as, for instance, where a surgeon or a nurse has had a finger deeply pricked by an infected needle. The discovery of the spirochaete may help us here. We may admit that if the parasite gain access in the first instance to deep tissues, or to veins, it may infect the blood without involving the overlying parts. A sore and an induration are possible only in skin or mucous membrane.

A young officer in the army was brought to me covered with a papular syphilitic eruption. It occurred also on his glans penis. He made no secrets and admitted exposure ten weeks ago and again eight weeks ago, but he had never observed any sore. He was liable to slight balanitis at times, but was careful in washing in order to prevent it. The most careful search failed to discover any trace of chancre, nor, what is perhaps yet more important, could any enlarged glands be found anywhere. The inference seemed to be that the virus had been absorbed in connexion with a slight balanitis and without the production of any sore. I might cite many such cases.

The omission of the bubo, although infrequent when the chancre is definite, whether it be indurated or otherwise, will be witnessed in a few cases. Ricord wrote, 'no syphilis without bubo,' but the assertion was in advance of the facts. Quite recently we had under observation at the Polyclinic a man whose indurated chancre was large, ulcerated, and of extreme hardness, and attended by an eruption. His groins were examined by the skilled fingers of a dozen observers, but no one could detect enlarged glands.

The omission of sore throat in the secondary stage, although less frequent than that of the eruption, is still fairly so. At the present day, when early and efficient treatment is the rule, it is impossible without great risks of fallacy to construct statistics as to syphilis, but my impression is that fully one-fourth of our English patients suffering from constitutional syphilis never show any definite sores on the tonsils or pharynx. In warm climates the omission of sore throat is probably still more common. For long it was asserted that the absence of sore throat was a distinctive feature between European syphilis and the framboesiform ‘parangi’ met with in Ceylon. My own investigations in Colombo convinced me that sore throats are just as common there in ‘parangi’ as they are in syphilis in Europe. In both countries many escape.

The troubles of the suppurated bubo, which formerly used to be the main terror of syphilis to our youthful reprobates, have, under modern treatment by iodoform externally and mercury internally, almost ceased to attract attention. They do, however, certainly occur occasionally, and not by any means exclusively in association with soft sores. Most undoubtedly the sclerosed sore of syphilis, although comparatively free from suppuration, is not always so. Pyogenic organisms often attend it, and when these are present the inguinal glands may pass beyond the bullet type, may become agglutinated, and may suppurate. A patient now under my observation with syphilitic eruption has large masses of adherent glands in both groins and suppuration is imminent. In another the glands from both groins have been excised on account of abscesses, but he has now abundant secondary symptoms in proof that the sore was an infective one.

The statements made in the preceding paragraphs may suitably warn us against the attempt to construct hard and fast rules as to the evolution of syphilis. Such rules will encounter constant exceptions, and they will mislead disastrously those who, without opportunities for personal observation, trust to them. I am much mistaken if the careful study of the facts will not further lead to the suspicion that the supposed distinctions between hard sores and their sequelae and ‘soft sores’ and their sequelae have not been drawn much too definitely. In practice a large majority of sores on the genitals, derived from venereal contagion, and which persist for more than a fortnight, whether indurated or not, lead to syphilis.

Some practitioners are fond of the assertion that syphilis is never really cured. ‘Once syphilis always syphilis’ is an expression which, thoughtlessly used, has caused lifelong misery to thousands. There is, it must be admitted, a sense in which it is true, but as applicable generally it is fortunately a cruel falsehood. A vast majority of those who have passed through an attack of syphilis, under judicious treatment, or even without it, get well and remain well through the rest of their lives. A certain vulnerability of tissues is no doubt left behind by all specific forms of illness. The influence of what is past is never wholly obliterated, and the human body that has been submitted to the influence of small-pox, scarlet fever, or even measles, never returns to precisely the same condition of soundness which it had before. Each may in turn be the cause of chronic maladies which would not otherwise have occurred. It is the same with syphilis, with the difference that its sequelae are more conspicuous and much more easily traceable to their cause. It may be admitted also that they are both more common and often more severe, but these admissions do not invalidate the assertion that for all practical purposes syphilis is curable, and that the great majority of its subjects remain wholly free from any reminders of their malady. The evidence in support of the assertion that syphilis is curable is obtained from various sources. We have first the experience of practitioners who have lived long enough to know what has happened through long series of years to those whom they have themselves treated for syphilis. Even without much regard to the stage at which the patient may have come under observation, this kind of experience will, I believe, be generally found to have been most satisfactory. Next we have the great frequency with which patients who come under care for other and quite independent maladies will, if questioned, admit having had syphilis in youth. We may note, also, that the total of such maladies as general paralysis and tabes, known results of syphilis, is small almost to triviality in ratio with the general population and the number who may presumably have suffered from syphilis. The very small actual mortality which results from syphilis is a fact pointing in the same direction.* The experience of certain nations and races in which syphilis is known to have been very prevalent for ages is also worth quoting. Spain and Portugal perhaps stand foremost in this matter amongst European nations, but their experience is far outstripped by that of the Fiji Islanders. In Fiji syphilis has prevailed from prehistoric times, and so almost universally that it is said that mothers prefer that their children should have it young and intentionally expose them to contagion. Yet although bone disease and lupoid affections of the skin are very common, the race as a whole remains a vigorous one. We have here an instance of self-curability on a large scale, for until quite recently neither mercury nor the iodides had been used.

The belief in the incurability of syphilis, held alike by certain sections of both the public and the profession, is, I am convinced, based upon narrow and erroneous observations. Those who have got well and remain so do not go about boasting of their cures and divulging their past, whilst the small minority who suffer are unable to conceal it. The number of the latter is vastly augmented in the popular creed by the common error attributing almost all forms of chronic skin disease to venereal taint.

Now that the prejudice against the long-continued use of mercury is rapidly disappearing, it may be confidently hoped that the remote sequelae of syphilis will become more and more rare. The newly-established principle of beginning treatment as early as possible will probably conduce to the same result. Leaving utterly aside the antiquated and most mischievous rule of practice which enjoined waiting for the appearance of secondary symptoms before commencing specific treatment, we shall be willing to prescribe the prompt use of mercury in all conditions of the primary sore which imply to the well-trained observer confident diagnosis. Even if such treatment be begun needlessly it will rarely, if carefully managed, be otherwise than beneficial to the patient. Mercury is helpful to many persons who do not suffer from syphilis, and hurtful to very few.*

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* I have for nearly thirty years held an appointment which brings under my observation large numbers of members of the public services. It might be thought that soldiers and sailors were likely to suffer from venereal maladies in at least an average frequency. As a fact, many cases of urethral stricture do come under notice. I can, however, scarcely remember one in which the existence of syphilitic taint has been held to prejudice the chance of average longevity.

A strong argument in support of the superiority of the small-dose treatment over all others is its freedom from risks and inconvenience. Writing of the virtues of atoxyl, M. Hallopeau in a recent paper puts the question whether the dangers involved in its use are such as to 'exclude it from our therapeutic arsenal'. He answers it in the negative, and alleges that practitioners do not hesitate to continue the use of mercury, '*larga manu*, malgré les accidents souvent graves, parfois mortels, qu'il peut entraîner.' Now of these accidents 'often serious and sometimes fatal' the small-dose plan knows nothing. All that is needful is to begin cautiously and increase gradually as the patient can bear it. The only inconvenience ever encountered is diarrhoea, and that is easily prevented.

The small-dose plan begun early and continued without intermission over a very long period is so efficient and so free from all drawbacks that its advocates are almost excusable if they show no zeal in the search for other remedies or other modes of the use of mercury. They may well be content to watch the results of experiments made by others. They find it difficult to conceive of any method which shall be either less inconvenient or more trustworthy.

* A patient who had taken a long course for unquestionable syphilis found himself relieved also of other maladies, and expressed himself as very grateful. 'Before I had syphilis my life was a burden to me, now I ail nothing.' He even expressed a wish that one of his brothers, who he said suffered from sick-headaches as he himself had done, might have syphilis and its treatment.

Jonⁿ Hutchinson

INTRODUCTION

BY

The late Sir JONATHAN HUTCHINSON, F.R.S.

THE HISTORY OF SYPHILIS

BY

DR. IWAN BLOCH

CHARLOTTENBURG, BERLIN

THE HISTORY OF SYPHILIS

CHAPTER I

THE BEGINNING OF THE DISEASE IN THE OLD WORLD ITS INTRODUCTION FROM THE NEW WORLD

A QUARTER of a century has elapsed since the vexed question of the origin of syphilis was first critically discussed by Montejo y Robledo, a Spanish army surgeon, at the fourth meeting of the International American Congress held at Madrid in 1882. Dr. Montejo[1] had occupied himself for a long time in investigating the origin of syphilis, and he communicated the results at which he had arrived to the International American Congress because he recognized that the recent origin of this disease was especially connected with America.

The information gathered by Montejo was gained almost exclusively from Spanish sources. He made an exhaustive collection of his authorities, collated them carefully, and examined them critically. But his work might have remained in obscurity if attention had not been drawn to it by Professor Seler,[2] in 1895, who had arrived at substantially the same conclusions about the appearance of syphilis in Europe as had already been deduced by Dr. Montejo.

Professor Binz, of Bonn, ignorant of Montejo's work, published a paper[3] on the occasion of the quater-centenary of Columbus in which he advocated the long-discredited view that syphilis in the Old World was a disease of comparatively modern origin which could be traced to America.

The admirable work of Montejo, Seler, and Binz deals with only one side of the question as to the origin of syphilis, their results being based mainly upon Spanish records. But the whole question to be answered is whether syphilis is a disease of modern origin or if it has always existed? Because if the modern origin is accepted and the antiquity of the disease be denied, the problem of its origin and introduction is solved at one and the same time. However much the interest of Americans may be bound up in the positive statements of Dr. Montejo, and whatever the amount of weight which should be attached to them, further consideration is necessary, as it is impossible to bring forward these alone as a complete and definite answer to the question. I have endeavoured in my work on the 'Origin of Syphilis'[4] to discover the other links in the problem and to demonstrate their connexion with each other, and I would refer the reader to that work for more detailed information and for documentary evidence which can only be indicated briefly in the present article.

There are two chief reasons which have made it impossible to dispel entirely the obscurity which surrounds the origin and the first appearance of syphilis in the Old World, in spite of the endeavours of such men as Astruc, Girtanner, and Hensler in the eighteenth century. The first reason is that historical criticism had not advanced sufficiently to unmask the stupendous mistakes and misstatements which had arisen in the course of centuries about a disease so widely extended and so much talked about as syphilis. In the second place, it was only in the latter part of the nineteenth century that the progress of medical science made it possible to obtain an accurate knowledge of the different forms of venereal disease. The history of these diseases and the statements concerning them appear, therefore, in a very different light to us from that in which they presented themselves to our predecessors. Thanks to improvements in historical criticism and to advances in the science of pathology, I believe that it is now possible to give a definite and positive answer to the question of the recent origin of syphilis in the Old World. All available statements and facts point to the last decade of the fifteenth century—particularly the years 1493–1500—as the time when syphilis first appeared in the Old World. There is not a particle of evidence to show that the disease existed in Europe before that time.

This is not the place to enumerate all the theories, hypotheses, superstitions, and fantastic conceptions which have been associated with the sudden appearance of this terrible disease. God,[5] man, and beast,[6] have been successively saddled with the responsibility for the scourge, and even the planets have been looked upon as the ultimate originators of syphilis, in accordance with the astrological superstition current in the science of the age[7] when the disease first attracted attention. Every form of incontinence, too, has been looked upon as the cause of the disease, in utter forgetfulness that unchastity was no new vice, and that it had long existed without giving rise to syphilis. Worse than these absurd fancies were those errors and half-conscious deceptions upon which was founded the belief that syphilis had existed in antiquity and during the earlier part of the Middle Ages—a belief which gradually assumed so dogmatic a form that it was subscribed to by such eminent medical historians as Heinrich Haeser and August Hirsch. It is now easy to expose the errors which led to the belief in the antiquity of syphilis in the Old World, and thus to demonstrate the futility of such a view. Conscious deceptions must be considered first, and, afterwards, that lack of definition which caused many different diseases to be classified together under a single general heading.

It has been said already that the first reliable information about syphilis dates its appearance to the year 1493, but certain contradictory statements appear in literature concerning its existence in earlier times. The most notable of these are the two communications of Franz Joseph Bodmann and Petrus Martyr, which considerably furthered the belief in the antiquity of syphilis.

Bodmann, in his 'Antiquities of the Rheingau' (Rheingauische Alterthümer), which appeared in 1819, reproduced a passage from the chapter records of St. Victor in Mainz which deals with a chorister who suffered from the 'mala Franzos'. These chapter records date presumably from the year 1472.

According to my investigations, which have been confirmed by Professor Karl von Hegel, this date, 1472, which has so long fascinated historians, was falsified by Bodmann, and was not originally contained in the document, which belongs to a much later epoch. It is known, indeed, that nearly the entire life-work of this strange man consists of forgeries in the most widely differing departments of science.

Within the last few months Dr. Herbert Meyer, lawyer and privat-docent of Breslau, has communicated the astonishing information that the so-called 'Provincial Law of the Rheingau' (Rheingauer Landrecht) has in reality never had any existence, but is one of the cleverest forgeries of this particular Bodmann, which for a century has duped lawyers and legal historians just as the falsified date 1472 has duped medical men—for in this year Bodmann asserted that syphilis was already known in Mainz.[8]

In the same category with Bodmann's forgery may be placed the celebrated letter which Petrus Martyr is said to have dispatched to his friend Pedro Arias Barbosa, Professor of Greek at Salamanca, and in which mention is already made of 'Morbus Gallicus'.

This letter, unlike Bodmann's forgery, was looked upon with mistrust even by earlier investigators. For Petrus Martyr describes as a layman, as early as the year 1489, symptoms of syphilis, and gives it the name with which the rest of the world only became familiar six years later.

The more recent critical investigators into the 'Opus epistolarum' of Petrus Martyr, from Leopold von Ranke to Jacob Bernays, have established the fact that the dating of the letters is purely arbitrary, that they are for the most part fictitious, and that, in particular, the letter to Barbosa could not have been written before 1508, since in this year a Chair of Greek was first founded in Salamanca.[9]

The second source of error was the lack of definition which for centuries prevailed in the conception of venereal contagion.

Up to the time of Ricord, i.e. at the beginning of the second half of the nineteenth century, the three venereal affections, syphilis, venereal ulcer, and gonorrhoea, were not clearly differentiated, but were thought to be fundamentally the same, whereas we now know that syphilis in particular, as a specific infectious disease with constitutional symptoms, has to be sharply distinguished from the other venereal disorders which only locally manifest themselves.

This early belief in the identity of all venereal affections was substantiated long afterwards, even by such an authority as John Hunter, who based his conclusions on experiments wrongly interpreted. This led to the historical side of the subject being treated from the same point of view.

If gonorrhoea and soft chancre were syphilitic in origin then syphilis had naturally always been in existence. Certain descriptions of and references to diseases of the genital organs by ancient and mediaeval authors could easily be taken as indicating syphilis. But a gradual recognition of the completely different natures of the three venereal affections showed these indications to be untenable. Their utter worthlessness can be realized in the light of modern dermatological development, which has made us familiar with a wholly new group of diseases, viz. the pseudo-venereal and pseudo-syphilitic. These are skin diseases which in part imitate, with deceptive similarity, the syphilitic syndrome. I refer only to those peculiar infective complaints, which, like syphilis, manifest themselves at the same time upon the body, the genitals, and in the oral cavity; such as certain forms of pemphigus, impetigo, herpes, and erythema exudativum multiforme. Other chronic skin diseases, too, can simulate syphilis in respect of localisation and appearance. To these belong, for instance, lichen ruber, which is not uncommonly present on the buccal mucous membrane and genitals as well as upon the rest of the body; psoriasis with the same distribution, &c.

This group of pseudo-venereal and pseudo-syphilitic diseases is exceptionally large, and even sixty years ago the clinical physician, Canstatt, realized that it furnished all the reputed cases of syphilis described by the older authors. It may be remarked in this conjunction that nowhere is any indication found that a causal connexion was recognized between disease of the genitals and a skin affection of the rest of the body and oral cavity before the date I have given.[10]

The fact that, in the entire literature of the Old World, both occidental and oriental, no description of the syphilitic syndrome anterior to the year 1495 is to be met with, whilst only from this date onwards does it rank as an independent disease, is happily substantiated by the results of the disinterment of bones.

Since the bones are the only portions of the human body which withstand under favourable conditions the ravages of time and maintain their original form after death, these dumb, but necessarily infallible, witnesses were appealed to for proof of the existence in the Old World of syphilis both in prehistoric and in historic times up to 1493. One single skeleton found in the whole range of the Old World which could be referred indubitably to a period prior to 1493, and which bore undoubted traces of syphilitic disease, would at once put an end to the whole discussion upon the age and origin of this complaint.

According to the adherents of the theory of the ancient origin of syphilis, it was to be expected that not merely a few, but very many bones showing syphilitic changes, would have been found in the Old World. What a mass of such evidence must the unbridled licentiousness of Imperial Rome and the excesses of the Middle Ages have provided, since, according to the opinion of these investigators, the nature of the then-existing syphilis was not recognized, nor, moreover, was it rationally treated!

It is to be expected, too, that the severest forms of bone disease in the nose and palate would be seized on and described by the exponents of this theory.

In reality, despite the most painstaking research from amongst the unnumbered thousands of remains of human skeletons of prehistoric, antique, or mediaeval origin it has not been possible to discover a single bone showing undoubted signs of syphilitic changes.

Virchow has repeatedly declared that no such pre-Columbian or prehistoric bone was known to him, and it is quite certain that no such bone is contained in either English or German collections or museums.

I had the opportunity of searching the ample Hunterian collection in London with reference to this point. It contains, amongst other things, numerous skeletal remains from mediaeval graves showing different pathological changes, but not a single bone with syphilitic lesions is amongst them. The same holds true of the collection in the Natural History and Anatomical Museums in Cambridge.

The statements of French investigators, notably of Parrot and Zambaco, upon the presence of syphilitic changes in prehistoric bones have not been verified by competent later investigators nor by those who are familiar with syphilitic bone-lesions, such as Virchow, Fournier, and Bayet. Parrot mistook rachitic for syphilitic changes, and Zambaco's case was a typical one of arthritis deformans.

It is, however, desirable that a thorough examination should be made of the morbid skeletons in the Paris museums. So far, Virchow's statement holds good, that no single undoubtedly syphilitic bone has yet been found, within the confines of the Old World, which dates from before the discovery of America.

'And yet', says the same authority, 'we frequently see bones from the uncivilized races in the most widely separated parts of the world, which prove most conclusively that syphilis spread amongst them after contact with Europeans. I need only call attention to bones from the Philippines, from New Caledonia, and from Australia.'

If we inquire when this first contact occurred, we are met with the surprising fact that it only dates from after the discovery of America, and, in particular, from after the outbreak of the great epidemic of syphilis at the end of the fifteenth century.[11]

This sudden outbreak of syphilis at the beginning of the last decade of the fifteenth century is the first undoubted fact, the starting-point from which investigation into the origin of syphilis can begin.

The campaign of Charles VIII of France during the year 1494–5, as a result of which many mercenary bands of considerable strength, accompanied by a great following of women, collected in Italy and there got into touch with one another, furnished the most favourable opportunity for the spread of such a disease as syphilis.

There can no longer be any doubt that syphilis first attracted attention in Europe when the French under Charles VIII sojourned in Italy.

The date thus determined for the first appearance of syphilis in epidemic form is that unanimously agreed upon by the contemporary chroniclers and medical authors of the most widely separated countries.

The greater number of contemporaries report that this occurrence took place during the stay of the French army in Naples, and therefore between February and May, 1495. Critical examination of reports of the period shows their unanimity in this, that they consider an invasion from without as having certainly occurred, and that they lay the blame upon the Spaniards. The Italian town chronicles enable one distinctly to follow the triumphal march of syphilis from town to town throughout Italy: everywhere the well-known dates 1495 and 1496 are given. By June, 1495, syphilis had already penetrated to the northernmost part of the Apennine peninsula, to the borders of France, Switzerland, and Germany.

The information as to the first appearance of this venereal disease is of the greatest weight, since it comes entirely from contemporaries who lived in contact with the sudden irruption of the complaint, and who must, in part, have borne traces of it upon their own bodies. Laymen and physicians are at one in asserting that the disease had previously been unknown in Italy ; all, moreover, took it for granted that it had been introduced from abroad. Its sudden mysterious appearance and its unknown nature caused the disease to make a profound impression everywhere, and to strike all men with horror.

This horror sprang, not so much from the complete ignorance concerning the new disease as from the fear which its severity and virulence spread abroad. The contemporary writers of every nation always paint the disease in the darkest colours.[12]

This malignity of syphilis can only be explained, according to our modern views as to the nature and manifestations of the disorder, on the supposition that all those races that have been attacked with corresponding severity had hitherto been completely syphilis-free. How otherwise can the severe phenomena observed at that time be explained, together with the early occurrence of the so-called secondary symptoms,—often even after a few days—the high fever, the intensity of the pain, particularly the unbearable arthralgia, the severe secondary skin affections (the so-called syphilitic small-pox), the frequently-occurring bodily decline, and, finally, the undoubted frequency of a fatal ending ? How could a reputedly ancient plague of mankind attack so many nations with such exaggerated intensity ? Again, it was not the case of a pestilence limited to a definite area, for which special causes could be held responsible, The fact is that the outbreak of syphilis which occurred at the end of the fifteenth century involved all European races and nations in the same degree and with the same virulence.

Even to-day we see, wherever syphilis is introduced into a virgin country, the same acute course, the same intensity of its manifestations, as in its first appearance in Europe.

The connexion of the above facts and events is obvious, and it leads us at once to the questions—What is the explanation of the sudden appearance of syphilis in Italy ? By what path did the scourge travel thither ? These questions include those of the real origin and of the most ancient home of syphilis.

The answer to these has already been given by contemporaries. Two main sources have to be considered in this connexion ; firstly, the reports of Spanish authors, to whom, as already mentioned, Montejo, Seler, and Binz have recently redirected attention ; secondly, the communications of Italian chroniclers.

Each source supplements the other so that they eventually settle the whole question.

Amongst the most important of the authentic reports of the Spanish authors are those of Diaz de Isla, Oviedo, Las Casas, Roman Pane, and Hernandez. But the most important witness in favour of the recent origin of syphilis is Ruy Diaz de Isla (1462–1542 ?). At the time of the first appearance of syphilis in Europe he had already passed his thirtieth year, was a physician, indeed a physician of note, and—last and most important fact of all, was himself a witness of the invasion of syphilis, which he observed to a certain extent upon its landing in Europe.

We know that Diaz de Isla was in practice in 1493 in Barcelona, later in Seville, and for ten years held the position of surgeon to the Hospital of All Saints in Lisbon. Here he acquired a large experience in syphilis, which he incorporated in a special work, the oldest edition of which, published between 1510 and 1520, was discovered by Montejo in the national library of Madrid. The title of this work runs: 'Tratado llamado Fruto de todos los Santos contra el mal de la ysla Española hecho por maestre Rodrigo de Isla cirujano vezino de lisboa para comun e general provecho de los pacientes Enfermos de la semejante Enfermedad que vulgarmente es llamado "Bubas",' i. e. 'Treatise, entitled, Fruit of All Saints against the disease of the island Española, by Master Rodrigo de Isla, surgeon and citizen of Lisbon, to the common and general good of those suffering from the disease in question, commonly called "Bubas".'

In the first chapter the origin and introduction of syphilis is exhaustively described.

This report contains facts of the author's own experience and own observation, and with one blow rends the veil which has covered the origin of syphilis.

The contents are briefly as follows:—

Syphilis was unknown in Europe before the year 1493. Its home is America, or, as far as Europe is concerned, the island of Española or Haïti, whence the crew of Columbus brought it after the latter's first voyage. Hence syphilis is called by Diaz de Isla 'Disease of the Island of Española'. By the Indians of Haïti, however, the disease is known as 'Guaynaras' or also 'Hipas', 'Taybas', and 'Icas'. The majority of Columbus's crew became infected there with syphilis and returned sick to Spain.

Diaz de Isla himself treated several syphilitic sailors from this squadron in Barcelona, and mentions amongst others the pilot Pinzon of Palos as one of those smitten with the new scourge. The complaint was quite unknown to the sailors themselves.

After the arrival in Barcelona of Columbus in the year 1493, syphilis spread there amongst the inhabitants, whilst yet Ferdinand the Catholic and Isabella were present. In the following year, 1494, Charles VIII of France began preparations for a great campaign and attracted mercenaries from neighbouring countries. Amongst these were many Spaniards infected with syphilis. Thus it came about that syphilis spread during the stay of the French army in Italy, and finally, through the combination of so many circumstances favourable to an epidemic outbreak, achieved that sudden and terrible diffusion of which we have learnt. Syphilis had been known in Española from time immemorial. At the time of Columbus's arrival the Indians were already in possession of a highly complicated, rationally developed and deduced method of cure of this ailment, the details of which Diaz de Isla learnt in the year 1504 from a translation. This consisted chiefly in treatment by means of guaiacum and other vegetable beverages, in conjunction with hydrotherapeutic, dietetic, and climatic methods of treatment.[13]

This classical record of Diaz de Isla is fully borne out by the communications of Oviedo and Las Casas.

Oviedo, a distinguished courtier, and one of those scholars frequently met with at the time, who even in early youth had acquired a many-sided culture, also found himself in Barcelona at the time of the return of Columbus in the year 1493.

He struck up a friendship with the son of the discoverer and acquired much useful information concerning the New World from Columbus himself and from the brothers Pinzon. Later he was for some time in Italy, shortly after the campaign of Charles VIII, and moreover spent several periods of a year each, in the New World, in Haïti, and Central America.

His communications upon syphilis are chiefly to be found in the thirteenth chapter of the second book of his great 'Historia general y natural de las Indias' (vid. pp. 50–6 of the Madrid edition of 1853), and further in an interesting report which he drew up at the command of the Emperor Charles V, and which is printed in Barcia's well-known collection.[14]

These reports show the complete accord of Oviedo with Diaz de Isla in relation to the American origin of syphilis.

Oviedo declares it to be a specific disease of the Antilles and Central American continent.

According to him, syphilis was communicated to the first Spaniards who came there with Columbus by the Indian women, and brought by them to Spain, whence it soon spread abroad upon the occasion of the campaign of Charles VIII. The name of the disorder should be West-Indian disease, rather than French or Neapolitan disease.

Amongst his informants, whom he questioned immediately after their return, Oviedo includes both those who accompanied Columbus upon his first journey and those who were with him on his second.

Amongst the first he mentions in particular the pilot Vicente Yañez Pinzon, one of the three brothers Pinzon. This is a remarkable and exceptionally valuable confirmation of the statement of Diaz de Isla, for the latter also mentions a Pinzon whom he saw with the first fleet of Columbus in Barcelona, to whom he spoke and who, like many other participants of the first voyage, brought back syphilis from the New World. It is highly probable that this Pinzon is identical with the one mentioned by Oviedo.

The preface to the report by Oviedo to the Emperor Charles V is noteworthy. He says there with emphasis: 'Your Majesty may take it as certain that this disease has originated in the West Indies and is common amongst the Indians, but in those regions is not so dangerous as with us.'[15]

Oviedo in his large work upon the West Indies has, as is recognized, attempted, in the interests of the Spanish conquerors, to justify their terrible treatment of the natives. For this purpose, some historians suggest that he invented the fable of the American origin of syphilis.

The weakness of this argument is demonstrated by the obvious fact that the noble Las Casas, the opponent of Oviedo and the friend of the Indians, also testifies to the American origin of the disorder.

He, too, was contemporary with the introduction of syphilis, his father even accompanying Columbus on his second journey, whilst he himself, as early as 1498, at the age of twenty-four, went to Haïti, where, after many voyages in Central and South America, he took up permanent residence and wrote his famous 'Historia general de las Indias'.

In vol. v, chap. xix, of this work (Madrid edition of 1786, p. 233), he says of Haïti :—'There were, and still are, two things which at the beginning were very dangerous to the Spaniards. One is the disease syphilis, which in Italy is known as the French evil.

'It is, however, known for certain that it came from this island, either when, with the return of the Admiral Don Cristóbal Colón with the news of the discovery of the West Indies, the first Indians arrived, whom I saw myself in Seville, or it may be that certain Spaniards were already tainted with this disease at the time of their first return to Castile. And as at that period King Charles of France went with a great army to Italy to invade Naples, and this contagious disorder spread throughout the forces, the Italians believed that they had acquired the disease from these soldiers and therefore gave it the name of "French disease".

'I took the trouble upon several occasions to interrogate the Indians of this island as to whether this disease was of great antiquity, and they answered "Yes", that it dated from a period long before the advent of the Christians, the origin of it being beyond the memory of any man, and nobody can disbelieve this.

'It is also an undoubted fact that all Spaniards addicted to sexual excess, who did not in this island observe the virtue of continence, were attacked by the disease, not one in a hundred escaping, unless the woman was healthy.' Las Casas also draws attention to the severity of the symptoms of the disease in the Spaniards compared with its mild course in the natives.

We see, therefore, that the reports of three contemporaries, widely sundered in their spheres of life, and opposed in their political views, unanimously proclaim the fact that syphilis is of American origin. And it was the syphilis in Haïti which was the unhappy source from which the poison was shortly to stream throughout Europe and the Old World.

In relation to syphilis in Haïti there is an interesting record of the Hieronymist Father Roman Pane which has survived and is printed in the 'Historia del Almirante de las Indias Don Cristóbal Colón' (Madrid, 1749, p. 63, col. i). It deals with the syphilis of the Haïtian national hero, Guagajona, and describes the Indian sweating cure, which is carried out in a remote place.

This locality, set apart for the treatment of syphilis, is called by Roman Pane 'guanara'. This is the same word as that mentioned by Diaz de Isla as the designation of syphilis and of things connected with it. This agreement is a conclusive proof of the value of the two documents, since each author makes his record independently of the other.[16]

The pre-Columbian existence of syphilis in the Antilles makes its presence on the adjacent mainland of Central America, ipso facto, probable. The researches of Montejo and Seler have made us familiar with the communications of the Franciscan Father Bernardino de Sahagun and the physician Francisco Hernandez upon the existence of syphilis in Mexico.

Sahagun's records in his 'Historia general de las cosas de Nueva España' are founded upon the communications taken down by himself verbatim from the natives, and that in the Aztec language, since he always laid the greatest stress upon the confirmation of truth.

Two passages come specially under consideration. One is found in Book X, chap. xxviii, where syphilis is mentioned under the designation 'Nanavatl', two varieties of this being distinguished—'Tlacaçolnanavatl', and 'Tecpil-' or 'pochonanavatl', which Jourdanet translates as syphilis with large and small pustules. According to this, the ancient Mexicans had already correctly distinguished the severe form of large pustular syphilides from the less malignant variety with small pustules.

In the same place Sahagun makes interesting statements concerning the Aztec therapeutics of syphilis; it was mainly treated by them with certain internal remedies compounded of vegetable drugs.

Still more important is the second chapter of the seventh book of Sahagun's works. Here syphilis plays a part in the Mexican myths, which undoubtedly have come down from ancient heathen times. Seler rightly remarks that through this fact the above-quoted passage from Sahagun acquires a totally different connotation. This chapter deals with the illumination of the world by sun and moon, and the future sun-god is here described as 'Nanavatzin', i.e. 'the little syphilitic', in Spanish 'el bubosito', who has a pustular eruption upon the whole body and who, in order to be turned into the sun, springs into the fire.

The interpretation of this remarkable myth cannot be gone into here. For us this one fact is of greatest importance, viz. that syphilis is mentioned in pre-Columbian tradition. 'Nanavatl' is syphilis; 'Nanavatzin' is 'the little syphilitic', and at the same time the name of the god. The main symptom, too, of syphilis as a constitutional disorder, viz. the skin eruption, is distinctly described.

According to the researches of Seler, the sun-god is looked upon by the Mexicans as the main cause of venereal disease in general, the different varieties of which were well known to them.

A welcome addition to this description by Sahagun is offered to us in the great work upon natural history of the physician Francisco Hernandez, which also is founded on observations made on the spot, and, for the greater part, on the statements of the Indians themselves. In folio 111 of the Mexican edition of 1615 of his work upon the Mexican vegetable, animal, and mineral kingdom, from the aspect of natural history and medicine, he makes mention of the 'Syphilis-medicine' of the ancient Mexicans, and uses for this a derivative of the same word 'Nanavatl' which we found recorded by Sahagun as the designation of syphilis. The 'Syphilis-medicine' is called 'Nanavapatli'.

For further traces of syphilis in Central America reference must be made to the detailed communications of Montejo and Seler as well as to my larger work.

Again this important fact may be added, that throughout

America definite names for syphilitic manifestations are met with, whilst it is recognized that, in the Old World, upon its first appearance, lack of familiarity with the disease was responsible for the absence of any designation, and countless appellations, many of them absurd, were artificially coined.

Each nation, too, named syphilis after the nation or country from which it first received the disease, e.g.—the Indians and Japanese called it the Portuguese disorder, from its introduction by the Portuguese ; the Russians called it the Polish disease ; the Turks, the Frank disease.

Montejo and Seler have therefore rightly ascribed a great importance to the definite nomenclature amongst the American aboriginal races as bearing upon the antiquity of syphilis in America.

Confirmation of the decisive narratives of Diaz de Isla, Oviedo, Las Casas, and others, concerning the origin of syphilis from America is obtainable from contemporary Spanish and Italian documents and chronicles.

Montejo was able to refer to documents in the Hospital archives of Seville bearing out the correctness of the statement of Las Casas that syphilis was introduced into Seville by the crews of Columbus, the most important point settled by him being that locally it was at once called 'Sarampion de las Indias', i.e. 'West Indian eruption'—a disease emanating from the West Indies.

The introduction of the complaint into Barcelona has been directly proved to us by Diaz de Isla and Oviedo.

We have, however, a third reliable witness of the propagation of syphilis in Barcelona even before the campaign of Charles VIII, in the person of the Italian humanist Nicolaus Scyllatius, who, in a letter of June, 1495, from Barcelona, gives intelligence of the syphilis epidemic which had existed for a long time in that place and as a result of which many inhabitants had been affected. This epidemic was stated to have existed for considerably more than a year in Barcelona.[17]

Finally many contemporary Italian chroniclers assure us of the introduction of syphilis from America by way of Spain.

Thus it is stated in the Sicilian annals, as early as 1498, that syphilis had broken out in Naples, which had been visited by Spaniards who brought the plague with them from the West Indies.

Senarega even states categorically, in his history of Genoa, that syphilis had appeared in Spain two years before the campaign of Charles VIII, i.e. in 1493, where it had been introduced from the Far West.

The contemporary Italian physicians, Alexander Benedictus and Antonio Benivieni, also declare that syphilis came to Italy from Spain. Many other chroniclers give the same information.

The circumstance is also illuminating that Spanish physicians were sent for to Italy for the cure of the disease, as possessing greater experience in the treatment of the new complaint than the Italian practitioners.[18]

CHAPTER II

ARGUMENTS AS TO THE PRE-COLUMBIAN ORIGIN OF SYPHILIS

Even if the facts enumerated above were not known to us, the mere examination of the oldest histories of syphilis in the individual countries of the Old World would amply suffice to prove its recent appearance in them, and hence to verify the fact of its introduction from the New World. Everywhere this disorder appears as a new disease, everywhere it is traced back to an invasion, and runs the characteristic malignant course already described. Since the era of its appearance coincided with that of the voyages of discovery it was soon carried into Africa and to the Far East, particularly by the Portuguese. It is a fact of great interest that the recent investigations of Okamura [19] and Susuki,[20] for China and Japan, as well as those of Jolly [21] and others for India, enable us to accept the recent introduction of syphilis into these countries as certain.

For the other European countries the years 1493–1500 are more or less accurately marked out as those which saw the introduction of syphilis, the same holding good for the individual towns. The great importance of the nomenclature of the new disease as bearing on the recognition of its recent origin has already been mentioned.[22]

As regards the introduction of syphilis into England and Scotland, the German writer, Grünpeck, as early as 1496, mentions the fact that English soldiers, fighting in Italy as mercenaries, acquired syphilis there, the probability being that some of them, on returning home, took the disease back with them. The first definite references to it are made in the year 1497.[23] The disease was introduced into Bristol in 1498 from Bordeaux and hence was called ‘Morbus Burdigalensis’. An

Old English MS. upon syphilis, dating from the end of the fifteenth or beginning of the sixteenth century (Sloane, 389, 7) exists in the Sloane Collection in the British Museum. The MSS. 157, 1 and 1897, 1 of the Sloane Collection, dating from the middle or end of the sixteenth century, also deal with syphilis. On page 80 of the 'Breviarie of Health' by Andrew Bord (b. 1480) is found: 'In English Morbus Gallicus is called the French pocks, when that I was young they were named the Spanish pocks.'

It follows that at the end of the fifteenth century, i.e. upon its first appearance, the true origin of syphilis was known!

In Scotland syphilis is first known to have existed in 1497.

An edict published in this year by the town council of Aberdeen refers to the appearance of syphilis in that place.[24] King James IV displayed great interest in the new complaint, being fond of experimenting in medicine, and treating people gratuitously, even paying them if they were not willing to be treated by him.

These entries are made between September and April, 1498, and in them syphilis is called 'grantgore' (à la grande gorre = à la grande mode).[25] On September 22, James IV published a decree ordering all persons suffering from syphilis to leave Edinburgh. They were to be taken to an island opposite Leith and there to be treated. Any of them found in the town were to be branded on the cheek.[26]

The celebrated old Scottish poet, William Dunbar, was at the time of the introduction of syphilis in 1493 in the bloom of manhood, and about the year 1500 was attached to the court of James IV by means of a state pension.

In a poem dedicated to the queen he makes reference to the new disease, which he calls 'pockis' or 'spanyie pockis'.

In another passage he writes :—

'Bewar with that perillous play
That men callis libbing of the Pockis.'

I have now to touch upon a question, the answering of which presents many difficulties, viz. that of bone discoveries in the New World.

A priori one would assume that syphilitic bones from pre-

Columbian times would necessarily be found there, whereby the diagnosis of syphilis as 'Morbus Americanus' could be established beyond all doubt.

I am of the conviction (which is shared by those who have an exhaustive knowledge of syphilis and its history, such as Unna, Scheube, Fournier, Liebermeister, Binz, and others) that the certain, irrefutable proof of the modern origin of syphilis rests upon nosological and epidemiological grounds; that the facts detailed amply suffice to prove its American origin; that the sudden transformation of the entire medical literature at the end of the fifteenth century furnishes the most complete explanation—but that positive bone discoveries would dispel every lingering and hidden doubt.

I cannot here discuss at length the extraordinary difficulties which present themselves in the diagnosis and differential diagnosis of syphilis from isolated bones; I have done this in the second part of my work on the origin of syphilis. To these difficulties in proving from bones the existence of syphilis in America in pre-Columbian times may be added the following.

In the first place, from climatic and other reasons, skeletal remains are hardly to be found in certain districts, which are precisely those under consideration. For instance, in Mexico only very few human remains have been discovered, with the exception of the north-west region, which is remote from centres of civilization. In the numerous graves of the province of Chiriqui in Colombia, according to Holmes,[27] 'human remains, almost without exception' were wanting. This is not only in accordance with the widespread custom of cremation, but may also be explained upon climatic grounds, e.g. the great humidity of Mexico.

Secondly, according to the records of Diaz de Isla, Oviedo, and Las Casas, it is certain that, in some districts at any rate, such as the Antilles, syphilis ran a mild course and bone lesions were rare.

Unna [28] and Scheube,[29] who have of late vigorously supported the recent American origin of syphilis, lay particular emphasis upon this mild course of the disease. The Mexican descriptions prove, however, that severe cases also occurred.

Thirdly, it is nearly always difficult to establish with certainty the pre-Columbian origin of the graves and mounds in North, Central, and South America. The same methods of burial and forms of graves survived for centuries after the discovery of America, hence it is rarely possible to pronounce a decided judgement upon any individual grave, as to whether it is or is not pre-Columbian.

I have, unfortunately, so far been able to undertake only a purely literary examination into the records of discoveries of syphilitic bones in America, as I have not yet had the opportunity of investigating these myself.

Several such bones, probably affected by syphilis, are to be found in the Musée Broca in Paris. The four skulls of children from Arica in Peru, in which Parrot maintained syphilitic lesions were present, are, in the first place, probably not of pre-Columbian origin, and secondly, from Parrot's own description, show only rachitic changes. Two other skulls of Peruvian adults, examined by de Quatrefages and Parrot, would appear to be suspiciously like syphilitic ones; the date, however, is uncertain. In the year 1880 Moreno showed at the Anthropological Society of Paris prehistoric skulls from Patagonia with manifestations of syphilitic osteitis, which were not accurately described.

The real discussion upon pre-Columbian syphilis in the bones of American aborigines centres round the remarkable discoveries of Joseph Jones in the mounds and graves of Tennessee. Of all the bones hitherto described they are the ones which most distinctly indicate syphilis. Jones's report appeared in the year 1876 in the 'Smithsonian Contributions' (pp. 49, 61, 65–73, 85). It described pathological changes in the extremities through periostitis, osteitis, caries, necrosis, and exostosis, presenting for the most part nothing specific. One skull, however, he declared, showed all the signs characteristic of syphilitic caries, particularly the eburnation of the surrounding bone; moreover, he found in another skull the thickening of the nasal bones which is likewise typical of syphilis.

On the ground of these discoveries, which at least arouse strong suspicion of the syphilitic nature of the lesions in question, Jones comes to the conclusion that 'the diseased bones which I collected from the stone graves of Tennessee are probably the most ancient syphilitic bones in the world'. This is of the greatest importance in the history of syphilis, as well as in the proof of its origin in the Western Hemisphere.

It must, nevertheless, be stated that both Virchow and Putnam, the latter of whom himself inspected the skeletons disinterred by Jones, do not agree with this conclusion, and view it with great scepticism. The pathologist Klebs, on the other hand, who inspected Jones's collection in 1896, entirely endorses the latter's opinion as to the syphilitic nature of these bones.

The main point of the whole discussion is, in reality, the question of the age of the graves in Tennessee. Their pre-Columbian character is by no means definitely established.

The same uncertainty concerning their syphilitic nature surrounds the pathological changes found by Prudden in a large number of pre-Columbian bones from Kentucky, and this also holds true of Putnam and MacLean's demonstration of syphilitic changes in skulls from the Morton collection in Philadelphia.

The description also by Ganns of a tibia with syphilitic changes found in a mound opened by him in Northern British Honduras, which he connects with a clay figure found at the same time, representing an operation upon the genitals, can, according to a friendly communication from Seler, only be looked upon with distrust. To begin with, here again the pre-Columbian character of the grave is not beyond doubt.[30]

In the opinion of Boas, Brinton, Seler, and others, a continuity between pre- and post-Columbian Indian civilization is demonstrable. Future discoveries, therefore, like those of Jones, conclusions from which may point with great apparent probability to syphilis, will bring with them the same difficulties in the way of a chronological decision.

The case is quite otherwise with the Old World. Here we are fully familiar with the great antiquity of the barrows, lake dwellings, and cave dwellings; with the ancient Germanic and

Slavonic cairns, even with the burial-places of the Middle Ages, and in none of them so far has a single syphilitic bone been found.

If, in the case of America, a verdict of 'Not Proven' must be entered, yet this difference between the Old and New Worlds seems to me essential. The opponents of the recent origin of syphilis, if they lay so much stress upon the osteological discoveries of the New World, are under compulsion to produce similar proofs from the Old. In this they have never succeeded and never will. But if we bring into relationship the above entirely unequivocal and well-established facts, the whole question is finally disposed of, for the historical investigator and historian of civilization, as well as for the thinking physician and pathologist. This, then, would appear to be the true solution of a 400-year-old problem, and one can say that, within the limits of scientific demonstration, it is the only possible one.

CHAPTER III

THE EARLY HISTORY OF SYPHILIS IN EUROPE

The appearance of syphilis was an epoch-making event for medicine and medical conceptions. Rousing the profession from the scholastic slumber of the Middle Ages, it confronted them with something new, which, because it arose so suddenly, called for comprehension and study of its peculiarities, while it made new demands upon clinical observation and diagnosis, and set a new task to practical therapeutics.

We recognize in the results of countless debates upon the nature of syphilis, and in the despairing attempts to bring its manifestations into line with the ancient schemes and rubrics of Galenical and Arabic medicine, how profoundly the appearance of this remarkable disease shook the theoretical and practical foundations and fundamental views of medicine as it had existed from ancient to mediaeval times. It checked the tendency to extravagant theorizing, and made unbiased observation a necessity.

Now for the first time began the really systematic study of 'venereal diseases', of which the purely local ones were known even to antiquity, such as gonorrhoea, local genital ulcers, condyloma acuminatum, &c. That their contagiousness was already recognized,[31] is proved by an interesting passage in the satires of Herondas, but this acquired a heightened importance in face of the appearance of a new constitutional venereal disease.

It must be emphasized that the earliest syphilographers separated the previously known venereal complaints entirely from syphilis. Gonorrhoea was at that time strictly defined. Paracelsus in 1530 first labelled it French gonorrhoea, and thus became the originator of the fatal error of the syphilitic nature of this disease, which lasted up to our own times. The gangrenous form of soft chancre too, the ‘ ulcus molle ’ so often described by mediaeval writers, which seems to have been extraordinarily widespread in that epoch, was not described by the earliest syphilographers as a symptom of syphilis, but was differentiated from it. Magnus Hundt has an interesting enumeration of local venereal affections, having nothing in common with syphilis. He mentions bubo, ulcerations, gonorrhoea, priapism, pollutions, pruritus testiculorum, ruptura penis, dolor ex retentione urinae.[32]

The first appearance of syphilis in civilized Europe attracted, as has been mentioned, the attention of physicians in a high degree, and even in the earliest years called forth a number of writings upon the new disorder.[33] No coherent description of the course of the disease, based upon accurate pathological knowledge, was possible, since prejudice in favour of the old theories concerning the nature of disease stood in the way. Already, however, most of the symptoms and appearances of syphilis had been described, such as the primary lesion, fever, pain, exanthem, alopecia, mouth and throat affections, disease of internal organs, of the nervous system, of bones and joints, &c. All authors dwell in particular upon the exaggerated intensity of the manifestations. This malignity of the disease, the early appearance of the secondary symptoms, the high fever, the severity of the pain, particularly the unbearable arthralgia, the appearance of the exanthem in the form of the severe ‘ variola syphilitica ’, and so on, can only be explained on the supposition that the scourge was a visitation upon nations hitherto syphilis-free. The heredity of syphilis was also observed by Paracelsus. Two methods of cure come under consideration : inunctions with mercury, and the wood-tea and guaiacum cures ; mercurial fumigations were already employed, in addition to internal administration of mercury, mercurial plasters, sulphur baths, and hunger cures.

Only the earliest founders of the scientific study of syphilis can here be mentioned, in the order of their enumeration by Proksch ; for further details the reader is referred to the latter's work and to that of the author : Marcellus Cumanus, Ulsenius, Grünpeck (1450–1531), Leoniceno (1428–1524), Torella, J. Widmann (1440–1524), Gilinus, Bartholomew Steber (1506),* Montesauro, Sebastian d'Aquila (1513–43), Villalobos (1473–1560), Schellig, Pintor (1423–1503), A. Benivieni (1440–1502), Brocardus (1500), Raut (1460–1508), Almenar, Cataneo, Alexander Seitz, H. Benedetti (1460–1525), John of Vigo (1460–1520?), G. Vella, L. Schmaus, Ulrich v. Hutten (1488–1523), G. Fracastori † (1483–1553), the originator of the name 'syphilis', J. Benedictus (1483–1564), J. de Béthencourt, P. Maynardus, M. Hundt (1449–1519), Paracelsus (1491–1534), Diaz de Isla (1462–1542), who treated the first cases of sickness in Barcelona in the year 1493, A. Ferri (1500–52), Rangonus (1470–1557), Roverelli, Summaripa, Thierry de Héry (1510–99), Brassavola (1500–55), Auger Ferrier (1513–88), Renner, and many others.[34]

The first correct views upon the syphilitic poison and its transference are found in the writings of Jean Fernel (1496?–1558), who was the first to insist upon the necessity of a lesion of the epidermis antecedent to a syphilitic infection and to deduce the general infection as occurring from the site of the primary inoculation.[35] The identification of local genital ulceration and gonorrhoea with syphilis dating from the middle of the sixteenth century prevented the pathological relations of the individual symptoms from being recognized.

This confusion is shown in the admirable writing 'De Morbo Gallico' (Padua, 1564), by Gabriel Fallopius (1523–62). He correctly distinguished, however, between syphilitic and non-syphilitic warts; bone-syphilis and gummata, as well as visceral syphilis, he referred to mercury. Fallopius was one of the first prominent opponents of mercury. He also recommended a variety of condom as a preventive of syphilitic infection. As a third eminent syphilologist of the second half of the sixteenth century must be mentioned Ambroise Paré (1510–90), who employed the speculum for examination of vaginal and uterine venereal affections, pointed out the indolence of the syphilitic bubo, and made the first detailed communication upon hereditary syphilis.

In studying the syphilology of the seventeenth and first half of the eighteenth century the tendency towards monographic treatment of individual portions of this subject becomes evident.[36]

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* See Plate I.

† See Plates III and IV.

Knowledge of the syphilitic infection and its mode of conveyance was increased by numerous observations. Gregory Horst (1575–1636), in 1628, reported nearly 100 cases of infection by cupping in Ulm, Bamberg, and Isny, and he, with the assistance of the Genevese surgeon Palfey, made the first communications on the inoculation of midwives and physicians from lying-in women and other patients (1718); Colle and Musitano (1635–1714) reported inoculation by kissing and from drinking-vessels.

So far as symptoms of syphilis are concerned, amongst the forms of primary affection were included at this time the so-called 'Crystallina' (bullae crystallinae), by which probably herpes genitalis was understood. S. Bazin and Peter Guenault described in the year 1628 induration as the surest sign of syphilis, and the significance of indolent buboes was also recognized. The different varieties of condylomata, on the other hand, were not yet clearly differentiated, and the knowledge of the syphilitic exanthem, of which Rondelet first described the 'corona veneris', was very imperfect.

In relation to the records of syphilitic affections of individual organs, may be mentioned the description by Musitano of chancre of the tonsil. Descriptions of nasal syphilis are particularly frequent (perforations, syphilitic ozaena). Schenk von Grafenberg and Severino by post-mortem examinations established the presence of specific syphilitic lesions of the larynx, windpipe, and lungs.

Of great interest are the investigations of Lancisi (1654–1720) upon the connexion between aneurysm of the heart and great vessels and syphilis, as presented by him in his work 'De motu cordis et aneurysmatibus'. Syphilis of the nervous system, also gummata of the brain, syphilitic neuralgias and diseases of the spinal cord were already at this epoch the objects of considerable attention,[37] whilst numerous descriptions of the manifestations and forms of bone syphilis were forthcoming.

Although to a certain extent it is only a compilation of current views upon syphilis, the celebrated work of Jean Astruc

(1684–1766) is valuable even to-day, because it constitutes an epitome of the knowledge of the period. It is entitled 'De morbis venereis' (1st edition, 1736; 2nd amplified edition, 1740, and numerous later editions and translations); it includes a discriminating bibliography of all previous writings upon syphilis and a critical historical examination into the American origin of the disease.

CHAPTER IV

THE LATER HISTORY OF SYPHILIS IN EUROPE

The history of venereal disease, which we have now followed down to the time of Astruc, is marked out into its principal stages from the middle of the eighteenth century to the year 1880 by the three names of John Hunter, Philippe Ricord, and Albert Neisser. The culminating point of the period of retrogression in scientific knowledge of syphilitic affections is certainly occupied by John Hunter, whilst the discoveries of Ricord and Neisser have paved the way for an exact knowledge of venereal disease which is in keeping with the general progress of medicine.

The doubts rightly cast upon the identity of the different venereal disorders in the eighteenth century, e.g. by Francis Balfour (1767), Charles Hales (1770), W. Ellis (1771), J. C. Tode (1774), Andrew Duncan, senior (1777), were unfortunately set aside for decades by the unhappy and misinterpreted experiment of the celebrated John Hunter (1767), which ushered in a period of decay in syphilology lasting until the appearance of Ricord.

Hunter inoculated himself on the prepuce and glans with the pus from a virulent gonorrhoea and produced a chancre as well as constitutional syphilis; from this he concluded that the secretion from a case of gonorrhoea was capable of producing both chancre and syphilis, and that the virus of all three diseases, gonorrhoea, chancre, and syphilis, was therefore identical.[38]

From further experiments[39] Hunter concluded that this single venereal poison could be transferred to the urethra and other mucous membranes as gonorrhoea, or to the skin as chancre, but that the blood and secretions of syphilitics were incapable of transmitting such contagion.

As a result of this unfortunate theory, the heredity of syphilis and the possibility of extra-genital inoculation, as by sucking, through drinking-vessels, instruments, &c., was simply denied.

On the other hand, Hunter established the non-syphilitic nature of the so-called 'acuminate condylomata' and emphasized their strictly local character.

The description of the induration of the initial sclerosis, whence this obtained the name of 'Hunterian chancre', had, according to Proksch, already been far better given by John Andree, Surgeon to the Magdalene Hospital in London, a contemporary of Hunter.

'Hunter', says Proksch,[40] 'dealt the most terrible blow to the doctrine of the involvement of the internal organs by syphilis. With a few calmly written lines he annihilated a doctrine which for three centuries had been proved upon countless bodies and accepted by all the physicians in the world. This doctrine had already led the great Morgagni so far that he was able in a series of cases to describe, with masterly capacity, the syphilitic affection of the cerebral arteries. Hunter merely said superficially: "I have not seen that the brain, heart, stomach, liver, kidneys, and other viscera have been attacked by syphilis, although such cases have been described by authors;" but this amply sufficed to cause visceral syphilis almost completely to disappear for more than half a century from the text-books upon venereal diseases.'

In the second half of the eighteenth century the Danish physician J. C. Tode (1736–1805) published by far the best monograph upon gonorrhoea, wherein, in opposition to John Andree, he deprecated early injections.

The knowledge of the sequelae of gonorrhoea was chiefly advanced by Morgagni. He described the results of an investigation into the pathology of Cowper's glands, cystitis, prostatitis, &c. John Andree devoted a particularly detailed description to epididymitis.

The great Morgagni (1682–1771) also published numerous valuable pathological observations on the bodies of syphilitic patients, and, in spite of Hunter's theoretical denial, adduced much reliable material in favour of the existence of visceral syphilis. He was the first to discover syphilitic disease of the cerebral vessels; described pulmonary syphilis, its complication with pulmonary tuberculosis, syphilitic bone affections, syphilitic laryngitis, syphilitic disease of the heart and great vessels, and 'lues cerebri.' Syphilis of the liver, spleen, and kidneys were also not unknown to him, as Valsalva, Baader, and others had already recorded cases.

Hereditary syphilis only found scientific recognition in the second half of the eighteenth century. Stoll, Plenck, and Nils Rosen von Rosenstein proved the existence of 'delayed hereditary syphilis', which to-day occupies so important a position; for the establishment of its recognition Sanchez[41] (1699–1783), Physician to the Court of Russia, laid down rules which guide us even to-day.

The therapeutics of syphilis was enriched by the internal use of sublimate, introduced by Van Swieten, after which the method of cure by salivation, hitherto employed, fell into discredit, a circumstance which ensures enduring honour for Van Swieten among all future observers. At the same time the so-called 'decoctum Zittmannei', after Johann Friedrich Zittmann (1671–1757), attained wide popularity, whilst opium, enthusiastically vaunted by J. D. Schöpff (1752–1800), had only a transient success.

In the history of syphilis, in addition to Sanchez, Girtanner, Gruner, and others, the name of Ph. G. Hensler[42] (1733–1805) stands out, his work being rich in interesting information on the venereal diseases of the Middle Ages.

Amongst the precursors of Ricord were many who, by unbiased and careful observation, paved the way for his conceptions, and who opposed, with criticism and scepticism, the erroneous teachings of Hunter, defended as they were by celebrated physicians and syphilologists such as Lagneau (1781–1868), Abernethy (1764–1831), Michel J. Cullerier (1758–1826), F. A. Walch (1780–1837), Petit-Radel (1749–1815), and A. G. Richter (1742–1812). Particularly to be mentioned are: Benjamin Bell (1749–1806), who maintained, in his work on gonorrhoea and syphilis,[43] the different nature of the gonorrhoeal and syphilitic viruses; F. X. Schwediauer (1748–1824), who enunciated the prophetic statement about the nature of the syphilitic poison: 'Fautil regarder ces germes de poisons animaux et ces particules contagieuses comme des êtres vivants ? ' ; Ernst Horn (1774–1848), with his decided declaration : ' Gonorrhoea in itself never produces chancre ; chancre, on the other hand, never gonorrhoea.'

Richard Carmichael (1779–1849) should be mentioned as a rival to John Hunter ; in contrast with the latter's single venereal virus, he imagined the existence of a large number, according to the skin affections they produced.[44] Thus, in his opinion, there existed a papular, a pustular, a phagedaenic, and other forms of virus.

The history of modern syphilology begins with Philippe Ricord[45] (1800–89), the great experimenter and pioneer. He began his researches early at the Hôpital du Midi, where he worked from 1831 to 1860, and in the years 1831–7 he performed 2,500 inoculations, by which he proved conclusively that inoculation of gonorrhoeal secretion in the most widely differing localities (urethra, vulva, vagina, uterus, rectum, conjunctiva) never succeeded in producing chancre or constitutional syphilis. He denied, however, the specific nature of the gonorrhoeal virus, and looked upon it merely as a simple catarrhal secretion, a point of view which was undoubtedly strengthened by the existence of what is now known as ' urethritis simplex '.

In syphilis Ricord distinguished three stages : firstly the primary stage, which begins with the chancre, auto-inoculable and in its ulcerating stage capable of giving rise to pustules, ulcers, or abscesses. The induration of the chancre is the expression of the passage of the poison into the organism, of the syphilis having become constitutional. In the second stage—the secondary—the syphilis, according to Ricord, is not contagious, but is already transmissible to the offspring. As the third stage, Ricord describes the encroachment of the syphilitic disease upon bones and viscera. Tertiary syphilis, he said, is neither contagious nor transmissible.

We are also indebted to Ricord for the important distinction between the ' chancre mou ' (soft sore) and the ' chancre dur ' (hard sore) ; for the discovery of the rarity of syphilitic re-infection ; for the description of vaginal and uterine chancre, opportunity for which was frequently given him through the use of the speculum, which he introduced for the investigation of venereal disease in women; and for the establishment of the fact that in supposed cases of constitutional syphilis following gonorrhoea, a hard chancre had been present in the urethra.

Ricord's epoch-making doctrines were supplemented by the experiments of J. von Waller[46] (1811–80) who, following an observation by William Wallace[47] (obiit 1838) proved the contagiousness of secondary syphilis by the actual occurrence of inoculation from the fluid of pustules. This was confirmed by F. von Rinecker[48] (1811–33), the so-called 'Pfälzer Anonymus',[49] and by the experiments of Guyenot,[50] being finally recognized by Ricord's pupil, Bassereau.[51]

In the year 1859 the contagiousness of secondary syphilis was publicly pronounced in the statement of a commission of the Académie de Médecine convened by Auzias-Turenne, and to which belonged de Paul, Devergie, Gibert, Ricord, and Velpeau, the conclusion being based upon four successful inoculations.

Further investigations into the different kinds of chancre were undertaken by Clerc[52] and Rollet,[53] who established the possibility of a combination of the different venereal infections, gonorrhoea with syphilis; soft chancre with syphilis; gonorrhoea with soft chancre; gonorrhoea, syphilis, and soft chancre. Rollet's 'chancre mixte' was an important discovery.

These results of clinical observation led von Bärensprung[54] to a development of the doctrine of duality, which, in contrast with that of the 'unitarians', maintained the impossibility of a true soft chancre ever changing into a hard syphilitic one; also that the induration of the latter was not the cause, but the result, of the general infection.

Adherents to this doctrine of duality were Lindwurm,[55] Karl von Sigmund, H. von Zeissl, A. Reder, F. Hebra, Rosner, Pietro Pellizzari, and others.

The idea of the so-called 'syphilization' promulgated in 1849 by Diday (1812–94), i.e. the cure of syphilis by repeated inoculations of the same infected person with syphilitic virus until immunity is produced, was particularly studied by Auzias-Turenne, who dedicated his whole life-work to this subject.[56]

Like his successors, Karl W. Boeck, Lindmann, Daniellssen,

&c., he failed to obtain any therapeutically valuable results. These studies, however, resulted in the knowledge that the products of syphilis are only rarely inoculable upon the patient or upon other syphilitic individuals.

The scientific foundation laid by Ricord for the study of the external clinical manifestations of syphilis, was utilised by R. Virchow in his celebrated treatise ‘Ueber die Natur der konstitutionellen syphilitischen Affektionen’.[57] He also shed the first light upon the peculiar periods of latency and recrudescence in syphilis, and established the fact of the passage of the syphilitic virus into the blood from the individual organs or tissues.[58]

The question, too, of the inherent difference between the soft and hard chancre could only be decided after the discovery of the specific micro-organism. Ducrey[59] had in 1889 isolated a bacillus from the secretion of the soft chancre which he regarded as its cause. Unna,[60] however, was the first to succeed in proving that Ducrey's bacillus was a transition-form of the real bacillus of soft chancre discovered by him, and which he named the ‘Strepto-bacillus’ from its arrangement in chain form.

Krefting[61] also found Ducrey's bacillus in pus from buboes. Later, Lenglet,[62] Besançon, Griffon, Le Sourd,[63] and Tomasczewski[64] succeeded in cultivating the streptobacilli artificially, and in producing soft chancres in man by inoculation with cultures of it.

Finally we have, in the last few years, arrived at the most important conclusions upon the nature and cause of syphilis. Metchnikoff and Roux[65] in 1903 succeeded in transmitting syphilis to monkeys, and on March 3, 1905, Fritz Schaudinn[66] discovered the origin of syphilis in a protozoon, the ‘Spirochaete pallida’, which numerous confirmations prove to be the undoubted cause.

These discoveries open entirely new prospects for the prophyaxis and treatment of syphilis, and the history of the disease herewith passes into a new and, it is to be hoped, a final phase.

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PLATE I

A

The title-page of Bartholomew Steber's treatise on Syphilis, published in 1497 or 1498. A Doctor of Medicine is represented examining the urine of a woman with a syphilide whilst the surgeon is painting the leg of a man suffering from an eruption of the skin.

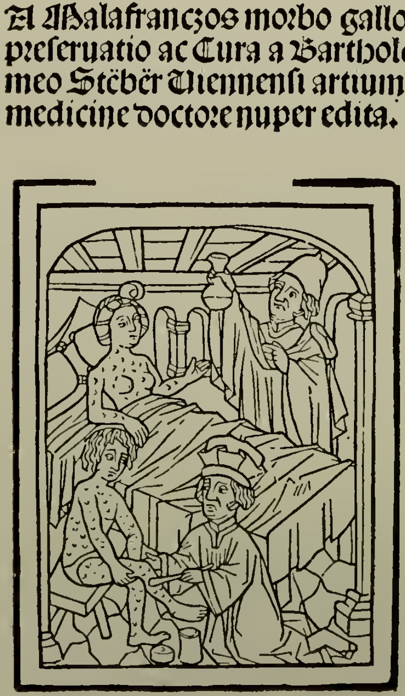
Steber was Professor of Medicine in the University of Vienna, Rector Magnificus in 1490 and Dean in 1492. He died in Vienna January 14, 1506, and is buried in the Stephanskirche in that city.

(This is probably the earliest illustration of Syphilis.)

B

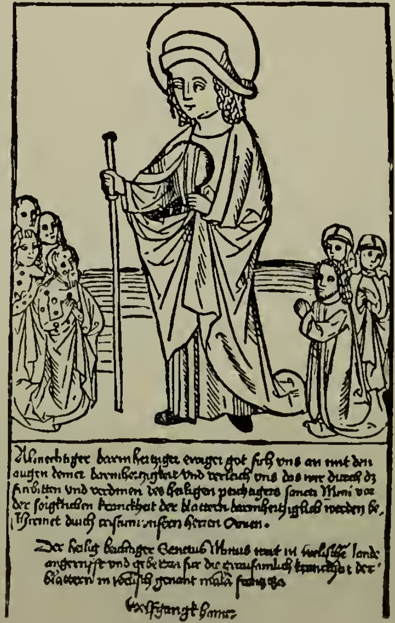
St. Minus (? Minias), the patron saint of those afflicted with Syphilis. The saint is represented staff in hand as a traveller, with his sleeve full of the healing roots he has cut with the sickle which he holds in his left hand. The patients he has healed, in the proportion of two women to one man, are kneeling behind him, whilst the sick, three women and one man, all with skin eruptions, kneel in front of him.

From a German print of the early part of the sixteenth century.



A Malafranczos moꝛbo galloꝝ
pꝛeſeruatio ac Cura a Bartholo-
meo Stëbër Viennenſi artium ꝛ
medicine doctoꝛe nuper edita.

A



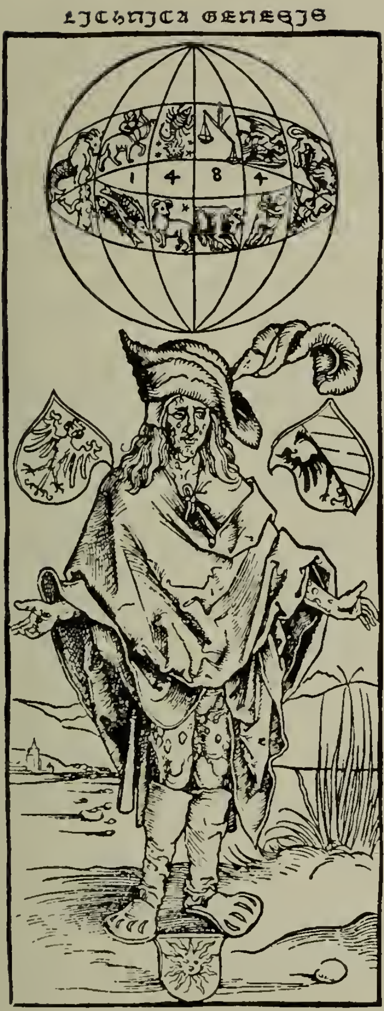
Allmechtiger barmhertziger ewiger got ſich vns an mit den
augen deiner barmhertzigkeit vnd verleich vns das wir durch dz
fürbitten vnd verdienen des heiligen peichtigers ſancti Mini vor
der ſorgklichen kranckhait der blattern barmhertziglich werden be-
ſchirmet durch criſtum vnſern herren Amen.

Der heilig beichtiger Sanctus Minus wirt in welſchem land
angerüefft vnd gebetten für die grauſamlich kranckhait der
blattern in welſch genant mala frantzoſa

Wolffgangk hamer

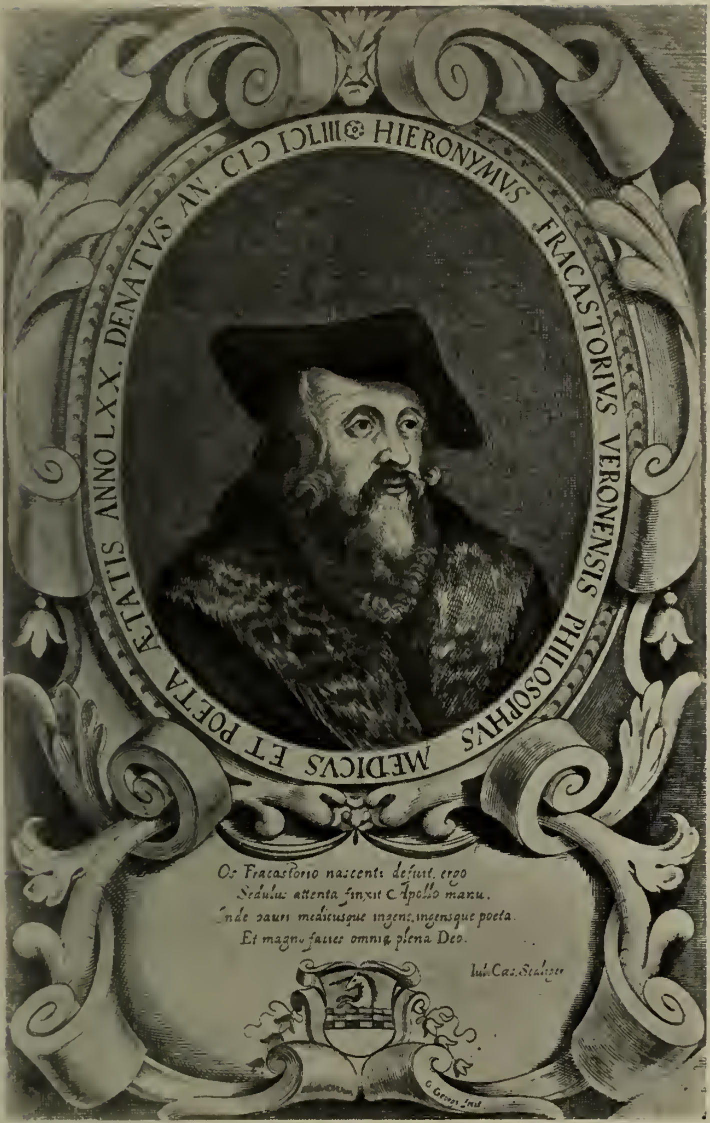
B

PLATE II



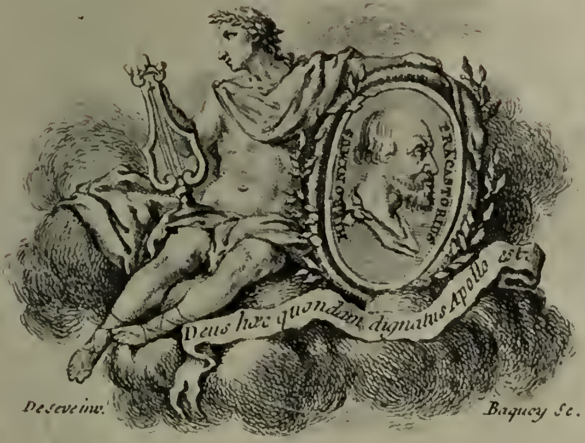
A drawing by Albert Dürer, forming part of the title-page of *Theodorici Ulsenii Phrisci Vaticinium in epidemicam scabiem qua passim toto orbe grassatur*, published at Nüremberg in 1496. The pamphlet is thought to be one of the earliest accounts of syphilis published in Germany. The drawing represents a man with an eruption on his skin.

PLATE III


HIERONYMVS FRACASTORIVS VERONENSIS PHILOSOPHVS MEDICVS ET POETA ÆTATIS ANNO LXX. DENATVS AN. CIↃ IↃLIII
Os Fracastorio nascenti defuit, ergo
Sedulus attenta finxit Apollo manu.
Inde sacri medicusque ingens, ingensque poeta.
Et magni facies omnia plena Deo.
Iul. Cæs. Scaliger
C. Gevers Inu.

Jeromo Fracastoro [1483–1553], poet, scholar, and Professor of Logic at Padua. He published his poem '*Syphilis sive Morbus Gallicus*' at Venice in 1530. The eloquence of the language, the melody of the rhythm, and the exquisite beauty of the digressions, stamped the poem a masterpiece, and quickly led to the general use of the word Syphilis to denote the new disease. The quatrain by J. C. Scaliger, printed below the portrait, refers to the fact that Fracastoro was born with his lips adherent to one another.

PLATE IV


HIERONYMUS
FRACASTORIUS
Deus hæc quondam dignatus Apollo est.
Deseve inv.
Baquoy Sc.

Tailpiece of Fracastoro's poem on '*Syphilis sive Morbus Gallicus*' published in Venice, 1530. The poem rapidly ran through many editions, and was translated into French, Italian, English, and German. To the popularity of this poem we owe the general acceptation of Fracastoro's term 'Syphilis' for the disease.

THE MICROBIOLOGY OF SYPHILIS

BY

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(Translated by J. Keogh Murphy, F.R.C.S.)

CHAPTER V

HISTORICAL ACCOUNT OF RESEARCHES ON THE MICROBIOLOGY OF SYPHILIS

The study of the Microbiology of Syphilis is a subject which presents very considerable interest, not only from the point of view of the sciences of microbiology and syphilography, but also because it cannot fail to attract the attention of every one who is interested in the progress of knowledge in general, and the progress of scientific research and deductions in particular.

At one period of medicine, when it was thought that most maladies were caused by disturbances in the functions of the organism, although some, at any rate, of our affections were admitted to have their origin from the outside world, it was generally held that contagious diseases were caused by some living agent which was easily transmitted to the perfectly normal human frame.

This was from the very first the case in syphilis, for it was seen that without any predisposition of the organism it was quite enough for some trace of specific poison to penetrate into our tissues, for man with certainty to contract the malady. It was thus quite natural to suppose that some microscopical organism was the cause of syphilis, and that this was capable of growth and multiplication in the human body.

Indeed, we can say that the microbiology of syphilis dates back to a period even before that of microbiology itself; for even at a time when we were still without a single precise idea with regard to the part played by microbes in fermentation, it was supposed that the real cause of syphilis was to be found in certain minute organisms which occurred in syphilitic lesions.

Indeed, no less than twenty years before the discovery by Pasteur of lactic acid fermentation, discussions were already taking place with regard to the microbiology of syphilis. Pasteur's labours showed clearly that fermentation is due to the activity of a microbe, and this discovery really opened the way to scientific microbiology.

In 1837, the same year in which the first attempts of Caignard, Latour, and of Schwann appeared, in which they explained alcoholic fermentation by the development of the yeast cells, a French microscopist named *Donné* published his microscopical researches 'as to the nature of various genito-urinary discharges in both sexes'. This work was very remarkable indeed, considering the time when it was written. Donné described certain miscroscopical organisms which he discovered in chancres, and which he compared to vibrios (*Vibrio lineola* of Müller, Plate V, *a*). Having observed these vibrios in vulvar chancres, Donné asked whether these 'animalcules' had any important rôle in the causation of syphilis. Struck by the fact that these vibrios could not be found in extragenital chancres, Donné endeavoured to clear up the problem by experiments. He produced suppuration in syphilitic persons, and in the pus thus obtained he never succeeded in seeing vibrios; thus he concluded that these organisms had no intimate connexion with syphilis, and that though his results made him still sanguine that a search for vibrios might be of service in the diagnosis of syphilis. Donné proceeded with great prudence and with strict scientific deductions only; thus he finally had to abandon his hypothesis that a vibrio, and *Vibrio lineola* in particular, was the cause of syphilis. In his 'Course of Microscopy', published in Paris in 1844, he expressed his opinion that the presence of these 'infusoria' was only a pure chance and had no constant connexion with the malady.

In this, indeed, he was perfectly right, though we cannot doubt for an instant that the vibrios found by Donné in syphilis were certainly not the aetiological cause of the malady. They are, indeed, only some of the many vibrios which develop secondarily in chancres of the genital organs, but are wanting in a great number of true syphilitic lesions: they probably correspond to the *Spirochaete refringens* of Schaudinn, according to the name now given to it.

We must remember that in Donné's time microbiology as a science did not yet exist. It is true that a certain number of microbes were known in the various secretions of the body, as well as in the external world, but there was no sure knowledge as yet of the rôle played by micro-organisms both in fermentations and in general diseases, nor was there any certain method which could reveal the presence of organisms in those parts where they are difficult to recognize.

In the first place, very great progress had to be made in microscopical technique before it was possible to approach so delicate and difficult a subject as the search for the organism of syphilis : indeed a period of nearly half a century was necessary to render the work of the smallest value.

As soon as Pasteur had definitely settled that micro-organisms had an important part to play in fermentation, the attention of medical men was at once turned towards the microbiology of infectious disease : again the discovery of so many new methods of microscopical research, due more especially to the work of R. Koch and Pasteur himself, at last stimulated scientific study of the aetiological agent of syphilis.

When once micro-organisms had been discovered in a whole series of different infectious diseases, it was natural that search should be made for them in some of the most contagious, such as variola and syphilis. Thus a great number of bacteriologists have applied themselves for more than twenty years to discover the cause of the latter malady.

The late pathological anatomist, Weigert, who was particularly distinguished for his discoveries in the methods of staining tissues and organisms, and who gave the first lessons in this art to Robert Koch, inspired considerable research into the bacteriology of syphilis in his laboratory in Leipzig. His pupil, *Lustgarten* of Vienna, in 1884, executed under his direction a series of researches which resulted in the discovery of a particular bacillus in different syphilitic lesions. This bacillus was known under the name of ' Lustgarten's bacillus '.

The work of this distinguished scientist of Vienna appeared in 1885,[1] and produced a very great impression by its scientific spirit and ingenious technique, as well as by the reserve with which he expressed his opinion.

By the aid of a method of staining closely resembling that used for the bacillus of Koch, Lustgarten succeeded in showing, both in indurated chancres and in syphilitic gummata, the presence of small bacilli, very fine and slender, closely resembling the tubercle bacillus. It was impossible to confuse these bacilli, however, with that of tubercle, as Lustgarten's organism could not be cultivated in any known medium.

This discovery was received in a very favourable way by the scientific world. It was confirmed by several observers, amongst whom Doutrepont and Schutz [2] should be particularly mentioned, and it appeared to be definitely established in science.

Although in the laboratory of the celebrated syphilologist, A. Neisser, no definite final pronouncement was made, the research of Marcuse,[3] proceeding from this scientific centre, confirmed Lustgarten's work and considered his bacillus as most probably the real cause of syphilis.

It is quite true that soon after the appearance of the work of the last-named Viennese syphilologist, Alvarez and Tavel [4] threw out the suggestion that the so-called bacillus of syphilis was nothing more than the microbe of preputial smegma, or of vulvar secretions which are to be found in healthy people ; for the general appearance, as well as the staining properties, were exactly the same in both kinds of bacilli.

After this statement the microbiology of syphilis was reduced to a study of the differential characters of Lustgarten's bacillus and that of smegma. Many workers, amongst whom we may quote G. Klemperer and Baumgarten, denied the identity of these two microbes, whilst others, notably Bitter, took an entirely opposite line.

Even if it were admitted that Lustgarten's bacillus, which was found in syphilitic products of the genital organs, was nothing but the ordinary microbe of smegma occurring in the same situation, there still remain those bacilli found by Lustgarten in syphilitic lesions of internal organs, where they could not be confounded with those of smegma as the latter could not have got into the depths of the diseased tissues.

It was now thought that the positive results of Lustgarten were due to a mixed infection in which the bacillus of tubercle was probably mistaken for the specific cause of syphilis.

The enthusiasm for Lustgarten's discovery did not last long ; in a short time it was evident that his microbe was very far from being constantly present in syphilis, and in those cases even, where it was found, there was plenty of ground for believing that its presence was due to secondary infection by a bacillus which had really nothing to do with the original cause of syphilis.

This discouraging result showed very clearly the difficulty of the whole problem, and made many distinguished bacteriologists relinquish the search ; but the discovery became all the more attractive to the most enthusiastic workers, men who never feared to face the greatest difficulties which microbiology could offer.

Thus we see, after the failure of Lustgarten's attempt, a series of works appearing in which many widely different varieties of microbes were presented as the causal agent of syphilis—some of them, it must be confessed, without any great reason.

Kassowitz and Hochsinger [5] described a streptococcus which stained by Gram's method as the cause of syphilis. Later, Disse and Taguchi [6] declared that the malady was due to a diplococcus surrounded by a capsule ; these multiplied rapidly in the blood of the patient, and were pathogenic for different kinds of mammalia, such as rabbits, dogs, and sheep.

Dr. Max von Niessen [7] has insisted for a considerable number of years that the best way to elucidate the cause of syphilis consists in sowing either the products of syphilitic inflammation or the blood of syphilitics on the middle of a culture. The germs which grow under these conditions are, according to him, different stages in the organism of syphilis. He finds the most widely different organisms. Side by side with orange and yellow micrococci are many different forms of bacilli and even fungi. Despite the efforts Von Niessen has made to persuade scientific men of the accuracy of his results by making many communications at different scientific congresses, and particularly in distributing his cultures, the general opinion is that these represent a general hotch-potch of every kind of impurity introduced into a nutritive medium. As far as the aetiology of syphilis is concerned, they are certainly not of the slightest importance.

In France, work of the same kind has been done by Dr. Quéry[8] who has cultivated many different kinds of micro-organisms from syphilitic products. These are just the same, and would appear to have nothing whatever to do with syphilis.

Amongst the bacteriological discoveries of recent years, those of Joseph and Piorkowsky[9] seem to agree best with the scientific requirements of microbiology. These inquirers also endeavoured to solve the problem by the help of cultures. But, considering very properly that ordinary methods could only bring them disappointment, they conceived an original and ingenious plan. Taking as a starting-point the fact of the infection of the foetus by a syphilitic father, they prepared cultures from a fresh human placenta sown with seminal liquid of persons affected with syphilis. By this means they obtained pure cultures of a bacillus, in which they believed they had found the specific cause of this disease. This organism was so distributed in the sperm of the patients that it was possible to isolate it in culture from no less than seventeen specimens of this secretion.

This same bacillus has, again, been found in cultures made from the blood of syphilitic patients, which fact has increased its value in the eyes of some scientists. At last, in the attempt to solve the problem, several doctors, themselves unaffected by syphilis, injected the bacillus of Joseph and Piorkowsky into their own arms. The negative result of this crucial experiment proved once and for all that there were no grounds for considering this microbe as the cause of syphilis. About this time De Lisle[10] commenced with great zeal to search in my own laboratory for the syphilitic micro-organism. After numerous experiments, carried out while taking into account the latest bacteriological work, De Lisle arrived at the conclusion that syphilis is a disease produced by large bacilli which were capable of cultivation on a certain nutritive media. Not being able personally to confirm this discovery, according to the etiquette of my laboratory I objected to its publication.

M. de Lisle then published it in collaboration with M. Jullien, without my sharing, in any way, their responsibility. It is very probable that he was dealing with some common organism which got into his cultivations through some mistake in technique.

It must be said, moreover, that no one has ever been able to confirm M. de Lisle's discoveries.

The search for syphilitic bacteria having completely failed, scientists had come to believe that they might be more correct in supposing that the microbe of syphilis is a protozoon. In a series of publications by Professor Stassano [11] it was said to be due to a flagellated organism capable of reproduction by multiple division (Plate V, *b*). Schüller, in a series of publications,[12] demonstrated that this disease is due to a curious micro-organism which appears in the form of corpuscles surrounded by stiff hairs; these were capable of reproducing by being changed into sacs filled with spores. The author even describes the cultures of his organism, obtained either from rabbits, or from cultivations from the incubator. The detailed description and the numerous figures in Schüller's publications do not allow us to judge of the nature of these corpuscles. Here we find represented very different objects, some of which recall grains of pollen or spores of truffles, whilst others have no resemblance to anything that we know. One cannot see why the author has imagined these things to be protozoa at all, nor why he has attributed to them the title of the organism of syphilis.

One can understand that under these circumstances Schüller's discoveries were not accepted by any one, and that his work only increased the profound scepticism which already existed concerning the problem of the cause of syphilis.

It was in this state of mind that scientists heard of a new discovery of a protozoon of syphilis. This time it was Dr. Siegel [13] who published an article in the 'Mémoires de l'Académie des Sciences de Berlin', in which he declared that the blood and exudations of syphilitics contained a small protozoon which is stained by a mixture of azur and eosine, and which, according to him, ought without doubt to be considered as the real organism of syphilis (Plate V, *c*).

Siegel gives it the name of *Cytoryctes luis*. The description and photographs in this memoir showed nothing which could in the slightest degree carry conviction to the mind of the reader. The photographs represented objects of uncertain shape, and did not resemble in the slightest degree any known form of protozoon. A great deal was said in the text about the ease of giving syphilis to rabbits and about the number of syphilitic organisms to be found in the kidneys of these animals. Although at the time of the publication of Mons. Siegel's book I myself was occupied in the study of syphilis, nothing seemed to me to point to the importance of this pretended 'Cytoryctes'. In my own mind I compared it to the hairy protozoa of Schüller. Without binding myself to go too deeply into research as to the aetiology of syphilis, I had been making some observations on my own monkeys, which had been infected by experimental syphilis. The resemblance of syphilis to dourine of horses, the parasite of which is well known, made us think that syphilis was caused by a trypanosome or some similar organism. When I met T. Bordet at the International Health Congress at Brussels, in 1903, he communicated to us the result of his researches in the microbiology of syphilis, made in co-operation with Gengou. These distinguished bacteriologists stained the syphilitic products with Kühne's carbol methylene, and afterwards with Nicolle's carbol gentian violet. By this method they found in an indurated chancre quite a large number of very fine spirilla, rolled like a corkscrew, and very faintly stained. These spirilla were found alone and not in association with any other microbe. Naturally, Bordet and Gengou were full of enthusiasm at this discovery, and continued the search for their spirilla in other cases of syphilis. But being unable to find this organism in five primary cases, either in the lymphatic glands of the groin, in the papules of the skin, or in the blood, they were discouraged, and did not pursue their investigations. It was only in a mucous plaque in the throat that they encountered the same spirilla, but as the throat, even in its normal state, contains very similar spirilla, they did not dare to attach any importance to their discovery. Despite this failure in the researches of Bordet and Gengou, and being fully alive to the difficulties I should probably find in my own way, I undertook the search for spirilla in syphilitic products obtained from my own monkeys.* In this work I was joined by *Levaditi*, who had a perfect knowledge of all the technical details of bacteriology.

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* The distinguished author omits to mention that in 1903, in conjunction with

Our first results were negative; we then thought that the best means of finding spirilla was to search for them in the small clear vesicles which sometimes form the primary lesion in the anthropoid apes. This form of lesion had been found by us more especially in the orang-outang. We obtained drops of clear exudation from these vesicles and examined them microscopically as suspended drops. As living spirilla are distinguished by their great motility, we believed that it would be easier to observe them by examining the exudate in a fresh state.

We were completely disappointed by our results; for the drops were always like a 'dead lake', and we were never able to observe the slightest movement in any of the minute particles which we found suspended in the fluid in great numbers. As a control we prepared hanging drops from the serum of fowls affected with spirillar disease; in these we could see without the slightest difficulty movements of the corpuscles caused by the spirilla, which were rushing about in all directions. The addition of a neutral red (Ehrlich's) stained the spirilla almost instantaneously, and they were then most clearly shown. The same stain added to syphilitic products never showed the presence of a spirillum. The methods of staining used by Levaditi gave the same result; in film preparations of syphilitic exudates we occasionally saw some few bacilli or micrococci which had got into the preparation by accident, but no spirilla.

After very many negative results, I was discouraged, and had not the energy to undertake a fresh research. Because of these results, Roux and myself, in our third 'Contribution on Syphilis'[14] ('Annales de l'Institut Pasteur,' 1904, pp. 661), expressed the opinion that the disease could not be attributed to any form of spirillum, but that it was probably caused by some non-motile organism. This view was soon to be proved to be erroneous, for it is indeed a spirillum that is the real aetiological cause of syphilis.

Roux, he first succeeded in inoculating a chimpanzee with syphilis; thus to their work we owe a large proportion of the recent advances in our knowledge of Syphilis.—TRANSLATOR.

CHAPTER VI

DISCOVERY OF THE SPIRILLUM OF SYPHILIS

Although Siegel's work produced little effect in most of the centres of research on syphilis, and though it was treated as yet another of the so-called discoveries of the organism of syphilis, in Berlin the work caused an actual sensation.

The members of the German academy of Science who had encouraged the author of *Cytoryctes luis* took great pains to show the truth of this work and to make it accepted by microbiologists. Franz Eilard Schulze, professor of Zoology at the University of Berlin, who is well known as the author of many important zoological works, was at the head of this movement. Thinking the whole matter to be of the greatest importance, he got together a commission of experts to study the question from all sides. *Schaudinn* was entrusted with the work, because he was considered one of the leaders in the study of Protozoa though he was still a young man. *Dr. E. Hoffmann*, a specialist in the study of syphilis, was associated with him in the work.

Their first care was to confirm Siegel's statement as to the presence in the blood and exudations of syphilitic patients of very minute organisms distinguished by their great motility. They very readily succeeded in proving that the so-called *Cytoryctes luis* was not really a micro-organism at all, but only some kind of organic débris like those found so often in all kinds of exudations. But at the very same time that they disproved this statement, Schaudinn found in the liquid taken from a syphilitic chancre some spirilla, exceedingly delicate in form, which swam about under the microscope with just the same movements which distinguish true spirochaetes.

An observer of such ability as Schaudinn, who had ignored the attempts of Bordet and Gengou which we spoke of in chapter V, could not fail to at once ask himself if this discovery of spirochaetes in syphilitic products was merely accidental and of no importance or if he had actually discovered the true organism of syphilis. The work being carried on in conjunction with such an experienced syphilogist as E. Hoffmann, enabled many of the early difficulties to be cleared away.

We must regard it as a very fortunate chance that in their very first case they were able to find quite a considerable number of spirilla. The patient was a woman aged 25 who had suffered for ten weeks from syphilis of the genital organs. She was seen by them on March 3, 1905, and was found to have a primary chancre on the left labium majus and several slightly ulcerated papules on the vulva. One of these papules was examined, and in its fluid Schaudinn[15] discovered motile spirilla in sufficient numbers to enable him to find one in every four fields of the microscope. When he tried to stain them it was found that the organisms could be shown by Giemsa's method, which consists in a mixture of methylene blue and eosine.

In a second case, which was that of a widow with secondary syphilis in the form of large slightly ulcerated papules of the genital organs, the members of the Commission—which had now been joined by Drs. *Neufeld and Gonder*—could only find very few and exceedingly fine spirilla. To make up for this, in a third case of condylomata of the genital organs, tonsils, and mouth, the organisms were found in great numbers. Thus we see that, as far as the number of spirilla present is concerned, Schaudinn and Hoffmann had better fortune than Bordet and Gengou, as well as myself, in my own first attempts.

The presence of these very slender spirilla, readily stained by aniline dyes, in the whole of a large series of cases of primary and secondary syphilis at once aroused the feeling that we might well be here dealing with the specific cause of syphilis.

From the very first, however, there was a great difficulty, which had of necessity to be cleared away as a preliminary.

Many observers at different dates had already found spirilla in lesions of the genital organs in man. Apart from the work of Donné, which I have already mentioned in chapter V, p. 44, large numbers of recent observations existed in the literature of the subject where the presence of wavy or spiral micro-organisms, found by different methods, had been noted. Thus Alvarez and Tavel [16] had found spirilla in the smegma, Berdal and Bataille [17] had found them in large numbers in the exudate from a case of ulcerating balano-posthitis. Later Rona,[18] of Buda-Pesth, had laid great stress on the spirilla which he had found in gangrenous lesions of the genital organs ; whilst, in spite of other observations, this author notes the presence of spirilla in nine cases of primary syphilitic lesions in man, although it did not occur to him to consider them as the actual cause of the syphilis, for he had already found the same spirillum in non-syphilitic lesions, and even in the normal genital smegma of both sexes.

Schaudinn and his fellow workers at once proceeded to attack the problem from this point of view. He examined for spirilla in different non-syphilitic affections, and he very soon found a large number in the exudation from a case of papillomata of the vulva in a woman aged 30 suffering from gonorrhoea, but having no sign whatever of syphilis.

We have already seen in the last chapter how hasty was the assurance with which some observers, but little qualified for a difficult research in microbiology, made their statements; on the other hand with what reserve those better qualified went to work —so much so that they were in the end too easily discouraged by the difficulties which came in their way.

We must consider it a particularly fortunate occurrence for Science that the discovery of the aetiology of syphilis fell into the hands of a man like *Schaudinn*, a zoologist by profession, who before this work had proved his ability by his research on the spirilla of birds and that of relapsing fever in man. From his familiarity with the characters of these particular micro-organisms, and as a result of patient inquiry, Schaudinn was able to announce that in the genital organs, both normal and diseased, two varieties of spirilla are to be found ; one of these is found in non-syphilitic affections as well as in some ulcerated syphilitic lesions, while the other is only found in syphilis. The first of these—which Schaudinn designated by the name of *Spirochaete refringens*—is much larger than the second; its spiral turns are fewer in number, although better marked than those of the second; it is readily stained by different methods, more especially by that known as Giemsa's; it is much more intensely stained than is the spirillum of syphilis. On the other hand, the second variety, called the *Spirochaete pallida* by Schaudinn, is much smaller as well as more slender; its spiral turns are more numerous, although not so marked; it stains with great difficulty by Giemsa's method as well as by other methods of staining; owing to this peculiarity it has been called the 'pale spirochaete of syphilis'.

Owing to his differentiation of these two varieties of spirillar micro-organisms in the genital organs, Schaudinn was able to overcome the first difficulty which obstructed his work; and by so doing he may be said to have taken the position by an actual *coup de maître*.

Encouraged by their results, Schaudinn and Hoffmann continued their researches on the aetiology of syphilis. They were first able to prove that the *Spirochaete pallida* is found in all cases of this disease and is never found in any other affection. In a very short time they had collected twenty-six observations in which they had always been able to show the presence of these pale spirochaetes; in some of these cases the organisms were wonderfully few in number, but they were always able at the end of the examination to find some specimens. On the other hand, in not one single case, be it venereal or otherwise, which was not syphilitic could the presence of the *Spirochaete pallida* be proved.

Continuing their work, Schaudinn and Hoffmann came to this conclusion, that 'true spirochaetes are to be found in fresh preparations, not only on the surface of syphilitic papules and of primary chancres, but also in the depth of the tissues and in the enlarged inguinal glands of syphilitic cases, diagnosed clinically; they are also found in film preparations stained by Giemsa's method. The question as to whether it is possible to establish differences between the parasites found in marked cases of condylomata and those of early syphilis can only be settled by further investigation.' This first communication was dated April 10, and appeared early in May, 1905.

Some days before this was published I received a letter from Schaudinn, dated May 2, in which he told me of his discovery, and asked me to send him films taken both from the primary lesions and from the enlarged glands of syphilitic monkeys. He told me the difficulty he had sometimes experienced in finding these spirilla, as he had actually at times only found a single example after a whole day's search. At the end of this letter Schaudinn expressed his opinion in the following words as to the two different varieties of spirochaetes : 'I have at the present time no doubt at all that the *Spirochaete pallida* is distinct from the other varieties which are to be found in the genital tract, although up to the present I can adduce no definite proof of my opinion.'

It now became of the greatest importance to collect all new work which might throw light on the problem of the aetiology of syphilis. Schaudinn, before he asked for preparations from my syphilitic monkeys, had already received films from indurated chancres in two lower species of monkey; these had been inoculated with syphilis by Dr. Kraus. But he found it impossible to find in them the *Spirochaete pallida*, in spite of all his investigations, though he used the proper method of staining.

Kraus himself gave me these preparations, and at the same time informed me that Giemsa's method ought to be used to find the organisms. As I had at the time two chimpanzees infected with most typical primary chancres, I endeavoured to search for the pale spirochaete, using Giemsa's method of staining. But the results were absolutely negative just as they had been in my original attempts (p. 51), and the preparations were in every case devoid of spirochaetes although they were examined by younger and more competent eyes than my own.

Although the results of our original investigations had made me abandon the search after the micro-organism of syphilis, this second time—having in view the twenty-six positive cases of Schaudinn and Hoffmann—I continued the examination of specimens from syphilitic monkeys. After many unsuccessful attempts we at last came across one case where the pale spirilla were very clearly to be seen. It was in a macaque (*Macacus cynomolgus*) (see Plate XVII) with a typical primary lesion on the eyebrow ;

this was covered with a thick crust, and on removing this a reddish serum escaped; which was found to contain a considerable number of spirilla. Soon after this we found the same organisms in two lower species of monkeys, and again in one of the two chimpanzees which had given us a negative result on the former occasion.

Encouraged by these results, we were able to find the pale spirilla in the cutaneous papules of secondary syphilis in man; these were far separated from the genital organs—that is, from those places where the larger spirillum refringens is to be found.

Having settled these facts, I sent some of my best preparations to Schaudinn: he confirmed my discovery, and begged me to publish my results as soon as possible. This I did in conjunction with Dr. *Roux* at the meeting of the Paris Academy of Medicine on May 16. In our communication we gave our views on the then aspect of the question in the following words: 'The collection of facts which we have now been able to put together pleads strongly in favour of the theory that syphilis is a chronic form of spirillosis caused by the *Spirochaete pallida* of Schaudinn.'

The presence of *Spirochaete pallida* in the beginning of chancres on the face and penis of monkeys, in association with other micro-organisms, shows us the importance of Schaudinn's discovery; while the proof that the spirillum is to be found in papules from their very commencement, and in those entirely closed in from the exterior, confirms us in our opinion.

Saling,[19] in his critical account of the microbiology of syphilis, reproaches me with the readiness with which I changed my first opinion as to the rôle taken by spirilla in this affection, and would attempt to explain it by some psychological reason. The matter is, nevertheless, very simple. My own original work was done before the discovery of Schaudinn, and here I was, perhaps, too much influenced by failing to find any spirilla in my own syphilitic monkeys, perhaps also not a little by the failure of such able workers as Bordet and Gengou. But when I myself succeeded in observing these spirilla enclosed in syphilitic lesions, far distant from the genital organs, both in monkeys and man alike, and this in the absence of all other organisms of any kind —this, added to the original work of Schaudinn and Hoffmann, proved at once to me that we had here a discovery of the very greatest importance.

The human syphilitic products which I had inoculated into my monkeys contained quite a microbic flora, in which spirilla, micrococci, and bacteria were to be distinguished. How, then, are we to understand that in the chancres produced by my inoculations I could only find Schaudinn's spirillum ? The other microorganisms, not being pathogenic, had been destroyed soon after inoculation, while the *Spirochaete pallida* had resisted all the defensive arrangements of the organism ! It must be true, therefore, that it possesses a particular pathogenic power.

Thus I modified my own opinion with a full knowledge of my reasons for so doing. This, I confess, is a psychological process which can rarely be done without regret ; one tries to take so many precautions to avoid error that it becomes very difficult to have to recant what has already been stated.

While we were clearing the way for our communication to the Academy of Medicine, we heard that a communication by *Buschke and Fischer*[20] was shortly to appear, describing the discovery of a pale spirillum in the liver and spleen of a child ten weeks old, affected with hereditary syphilis ; they added that, though these spirilla were very abundant, it was impossible to find any other organisms in association with them.

Now, while Buschke and Fischer took great care not to interpret their discovery as being in favour of the spirilla of Schaudinn being the cause of the disease, it must be clear that this made the balance turn very considerably in favour of the view which held that syphilis was a chronic spirillosis. At the same meeting of the Academy of Medicine at which we made our communication, *Levaditi* brought specimens from an infant with hereditary syphilis, showing that the bullae of pemphigus were full of pale spirochaetes.

The facts that we have shortly detailed in this chapter may be said to have laid the foundation of the microbiology of syphilis. Schaudinn's discovery is by far the most fruitful of all made before him. In every bacteriological laboratory, and in a large number of clinics, men have set to work with wonderful enthusiasm to find the *Spirochaete pallida.* Thanks to the perfection of their technique they have arrived at most accurate results, and in the short space of two years a quantity of facts has been accumulated about the microbe of syphilis which cannot be at all compared with the comparatively few we know about the bacillus of tuberculosis.

In this connexion it is worth noting that Lévy-Bing,[21] in detailing the literature of the *Spirochaete pallida* at the beginning of the present year 1907, mentioned 617 papers about this organism, whilst in the list of publications dealt with by E. E. Hoffmann,[22] completed up to December, 1906, the number was 750 articles.

Without entering too far into the subject of the microbiology of syphilis, I will content myself by giving the reader an account of the principal results we have obtained up to the present time.

CHAPTER VII

THE OCCURRENCE OF *SPIROCHAETE PALLIDA* IN SYPHILITIC LESIONS

As we have already seen, the spirilla of syphilis were first discovered in primary and secondary lesions of the genital organs. Soon after this their presence was proved in secondary lesions occurring in parts far removed from the genital organs; in syphilitic lesions in monkeys and in hereditary human syphilis.

At the present time, since our views about Schaudinn's spirochaete have grown in an extraordinary way, we can say, speaking generally, that this organism can be shown in every possible lesion which is definitely syphilitic. In the *primary indurated chancre* they have been found a great many times, and although we may meet occasionally with a typical primary lesion in which we search without success for these spirilla, such cases become more and more rare as our technique improves. Further, it is necessary sometimes to search for a very long time before we find a definite spirillum, and it is quite certain that many of those cases formerly described as being free from spirilla are to be explained by the entirely insufficient number of preparations examined in the investigation.

The same remarks apply to the *secondary lesions* in which it is sometimes impossible to find the spirillum. This has been more especially proved in the study of roseolar rashes. Very often we search in vain in these spots for the specific organism. But this does not interfere with our finding it in a certain number of cases.

Thus, Ploeger,[23] Bandi, and Simonelli[24] observed it in the blood of roseolar spots, while MM. Veillon and Girard[25] found it in sections taken from various roseolar spots, some of them of only a few days' duration. Spirilla have also been discovered in the *terminal capillaries* of the papillae of the skin, and in some deeper capillary vessels below the papillae; and whilst the majority of these organisms are to be found in the blood, some of them have been shown to have already penetrated into the peri-vascular tissue.

The facts I have just mentioned are far from being the only ones which demonstrate the presence of the spirilla of syphilis in the *blood.* Amongst others which more particularly prove this point are the observations of Noegerrath and Stoehelin,[26] who found a few spirochaetes in the blood of three persons affected with secondary syphilis, who had not undergone any treatment. Indeed the presence of these organisms in the blood has now been shown a great number of times. Schaudinn himself demonstrated the presence of syphilitic spirochaetes in the blood of the spleen obtained by puncture.

Although they are to be found in the blood, these organisms are still more numerous in the *lymph* and *lymphatic organs* in general. In their very first searches Schaudinn and Hoffmann (loc. cit.) observed the spirilla in film preparations taken from the femoral glands of their patients. A large number of observations soon confirmed this result, and although it is by no means rare to search in vain in preparations of these organs for the organisms in question, still, on the other hand, their presence in lymphatic vessels may be said to be constant in syphilis, and it is at times possible to see a very large number in the peri-vascular spaces, although their number in the corresponding blood-vessels may be exceedingly limited.

Apart from these lymphatic glands belonging to the special regions attacked by the primary lesion, the presence of Schaudinn's spirillum has been shown many times in those more properly belonging to the secondary period, as in the case of Levoendowski, who found them in the epitrochlear gland, the enlargement of which is so characteristic of syphilis.

The attempts to find the spirochaete in the *cerebro-spinal fluid* have already been many in number without giving very positive results, except in the case of Dohi and Tanaka,[27] who found Schaudinn's spirillum in this fluid taken from a patient suffering from papular syphilis. It is by no means astonishing that many other observers—amongst whom we may mention Widal, Ravout, and Siebert—have failed to do so, because the cerebro-spinal fluid has been shown, according to Hoffmann, to be free from any infective power except in very rare cases.

It is more astonishing that up to the present it has not been possible to demonstrate it in the *seminal fluid*, as this has been shown to be infectious by many experiments. Thus Finger and Landsteiner have obtained typical primary lesions in monkeys inoculated from the sperm of patients.[28]

It is not astonishing to learn that the *saliva* of persons suffering from syphilitic lesions of the mouth contains the syphilitic organism, although it is very remarkable to find that this fluid contains so many of Schaudinn's spirilla as Follet [29] would believe; this observer has stated that two or even three hundred specimens of the spirillum are present in each field of the saliva of persons who have not been treated by mercury. I must say, however, that in the preparations which Follet desired me to look at, I certainly saw a very large number of spirilla; but these belonged to many varieties, probably no less than four in number.

In the same way the presence of specific spirilla has been proved in the *urine* of persons infected with syphilis. Dreyer and Teuvel [30] have found them in the urine of a case of syphilitic nephritis; Maclennan [31] has described these organisms in the urine of a woman infected with syphilis, although it is true that he only found them in the neighbourhood of little corpuscles which he took for the *Cytoryctes luis* of Siegel, and on account of this the observations must be received with caution. It must not be forgotten that the female genital organs are the home of other forms of spirilla which may be at times mistaken for the *Spirochaete pallida.*

Now, although the presence of this organism has been proved without any great amount of difficulty by a great number of observers in both primary and secondary syphilis, it has not been the same in the case of *tertiary syphilis.* Here many observers have either reported a negative result or have given it as their opinion that the organism in tertiary syphilis is to be found in some form other than that of a spirillum. However, thanks to untiring labour and improved technique, more accurate results have been arrived at. Spitzer in 1905[32] was able to show the presence of small numbers of the *Spirochaete pallida* in gummata, both closed and ulcerated. Since this work, several other observers have obtained the same results in a fair number of cases.

Schaudinn found a mass of the organisms in the peripheral part of a gumma of the liver, occurring in a patient infected at the age of twelve. Hoffmann and Feldmann,[33] after laborious work, found isolated individuals in the peripheral parts of tertiary syphilides ; in the same way Blascke found them in a lesion of the scrotum occurring sixteen years after infection. Again, we may quote S. Dudgeon,[34] who found a number of the spirilla in a suppurating gumma of the jaw ; also the work of Doutrelepont and Grouven,[35] who succeeded in showing the presence of Schaudinn's spirillum in sections taken from four cases of tertiary syphilis.

The *vascular system* in general and the arteries in particular are very seriously affected by syphilis in its different stages ; it has therefore been exceedingly important to prove the presence of the organism of syphilis in specific arterial lesions of the tertiary stage. Reuter of Hamburg[36] found the organisms in sections of the aorta of an old syphilitic, who had died suddenly in the street, after suffering from cardiac trouble. Schaudinn has confirmed this observation by examining his specimens.

Now, although the presence of the specific organism of syphilis in cases of primary, secondary, and tertiary infection is by this time a definitely established fact, in those complaints which are called by the general name of 'parasyphilitic affections' the many investigations which have been made up to the present time have been of no avail. All cases of general paralysis and tabes studied from this point of view have shown themselves to be free of pale spirilla, or indeed of any form of spirillum.

Although it is not remarkable that the aetiological cause of syphilis was only discovered when many very favourable circumstances were present, more especially owing to the discoverer having started on cases where the organisms of syphilis were particularly plentiful, yet we cannot but be surprised that the pale spirillum had not been found in cases of *hereditary syphilis* before the work of Schaudinn. It is indeed amazing how large a quantity of these microbes are to be found in the foetus or newborn child infected with syphilis.

We have described in the preceding chapter the first cases of this affection in which spirochaetes were discovered. Since that time a large number of papers have been published on this subject, which, indeed, presents one of the very best worked out chapters in syphilography.

Although Schaudinn's spirochaete has not actually been discovered in seminal fluid, its presence in this secretion must be certain in many cases, owing to its infectious character ; there is no reason to suppose that the spermatozoa are infected by this microbe, it is more probably to be found free in the surrounding fluid. On the other hand, there exists definite proof of the penetration of the *Spirochaete pallida* into the *ovum.* Thus Levaditi and Sauvage [37] studied the ovary of a child aged one month, whose mother was infected. They not only found *Spirochaete pallida* in the stroma of the ovary, but they also found some of these parasites in the protoplasm of the young ova themselves.

Independently of this discovery Hoffmann and Wolters [38] have observed the organisms surrounding the ova of a foetus of seven months, and some of them even in the interior of the ova. Thus there is nothing impossible in believing that this is one of the means of the propagation of syphilis, although there is still no actual definite proof of the fact.

From this point of view it is interesting to note the presence of the organisms of syphilis in a case apparently free from the disease. Buschke and Fischer [39] studied a typical papular eruption in a new-born child. The mother presented no suspicious symptoms whatever, except perhaps a certain amount of alopecia. On closer examination an indurated inguinal gland was found. This was punctured and found to contain most characteristic spirochaetes.

The *placenta* has been found by many observers to be a resting-place for these organisms. Ménétrier and R. Duval,[40] Wallich and Levaditi,[41] Nattan-Larier and Brindeau of Paris,[42] Paschen of Hamburg,[43] Mohn of Leipzig,[44] all have proved their presence in the foetal placenta, though they are sometimes present in small numbers. Thus Wallich and Levaditi have only once been able to find them; on the other hand Mohn discovered them nine times out of thirteen. The umbilical cord has very often been found to be invaded by spirilla.

The authors just named have recognized that the spirilla found in the infected placenta always belong to the foetal and not to the maternal part; this agrees with the fact that these germs are only found rarely in the decidual membranes. The invasion of the foetal portion of the placenta is readily explained by calling to mind the extraordinary number of spirochaetes found in the tissues of a syphilitic foetus.

Thus, as we have just mentioned, the specific organism of syphilis is found in cases of *congenital syphilis*, very often in enormous quantities. While in *acquired syphilis* it would appear to be localized to the affected parts and its generalization seems to occur only in a very small degree, on the other hand in congenital syphilis this dissemination occurs to an extraordinary degree in both the organs and fluids of the body, which very often contain large quantities of the *Spirochaete pallida*. It has been found in the blood of the dead foetus, and also in that of the living child.

An observation of Buschke and Fischer[45] is of particular interest in this connexion. They observed a child six weeks old: it had not a single symptom of congenital syphilis, except perhaps some slight catarrh of the nasal passages, yet when examined clinically they found relatively large numbers of spirilla in the blood. Despite anti-syphilitic treatment, this child died, and at the autopsy very marked lesions of the liver and spleen, which were obviously syphilitic in nature, were found, and both organs were hypertrophied. Besides the blood, the liver, and the spleen, Schaudinn's spirilla have been found in the bile and in the deposit from centrifugalized urine.

We have drawn attention in Chapter VI (p. 58) to the discovery by Levaditi of numerous spirilla in the bullae of

Pemphigus neonatorum. Since that time a great number of observations has confirmed the fact, and they have been found not only in the liquid but also in the walls of the vesicles of pemphigus.

Without going into the question at length of other diseases of the skin and mucous membranes, we may say briefly that all the organs of a new-born child affected with syphilis have been shown to contain the spirillum. They have also been found in the superficial and deep lymphatic glands, in the liver (Plate VII), the spleen (Plates XIV and XVI), the lungs (Plate XV), the suprarenal capsules, and the pancreas. The thymus, the thyroid body, the testicles, and—as we have already mentioned—the ovaries.

In all these tissues a varying number of pale spirilla are to be found. Parts of the *skeleton*, such as the periosteum, cartilage, and marrow of the bones, have also been found to contain the organisms.

We should also note a peculiarly interesting fact—the presence of Schaudinn's spirochaete in the organs of circulation. In one case of a new-born syphilitic infant, who died of myocarditis, and was examined by Buschke and Fischer (loc. cit.), the quantity of these organisms was remarkably large ; the vessels and capillaries were surrounded by a thick mesh-work of spirilla, a certain number of them being found in the walls, as well as in the lumen of the vessels.

Thus it is not astonishing that, as far as aetiology is concerned, the study of the microbiology of syphilis has now come to occupy a very important position.

Side by side with this we must place *Experimental Syphilis*, a subject to which attention has already been directed. After the first proof of the presence of the *Spirochaete pallida* in syphilitic monkeys, a great number of new facts has been added to our knowledge.

It has been proved that the organism is to be found in all cases of primary infection, in anthropoid apes as well as in the lower orders of monkeys. Neisser, Baermann, and Halbenstädter in Batavia,[46] Finger and Landsteiner[47] as well as Kraus and Prantschoff[48] in Vienna, have proved this in a large number of cases. This observation, of course, is particularly important, in view of the fact that apart from Schaudinn's spirilla the experimental lesions in monkeys (which are usually produced in the eyebrow) do not contain any other organism—at least during the earlier periods of the infection. The lymphatic glands which belong to this region contain in just the same way the specific spirillum, as has been shown by Levaditi and Manouélian.[49]

The same spirilla have been found in most of the examinations of the papules and mucous plaques of secondary syphilis in anthropoid apes.

The question as to the presence of spirilla in the internal organs of monkeys has been much discussed. Neisser with his fellow workers having shown that certain internal organs such as the spleen and the marrow of bones contain infectious virus, the question naturally followed as to whether spirilla were to be found in these parts. This has been answered by Zabolotny,[50] who found spirilla which stained readily in the spleen of a syphilitic monkey. He gave a demonstration of them at the Congress at Berne in 1906.

Lately several observers have published very interesting observations as to Syphilitic Keratitis, which was produced in rabbits and dogs by inoculating them with syphilitic products from men and monkeys. Bertarelli [51] was the first to show the presence of a large number of absolutely typical spirochaetes in these ocular lesions in the rabbit. This discovery has already been confirmed several times, amongst others by Hoffmann, who, working with Brüning [52] has added a new observation, that when a fragment scraped from an indurated chancre is inoculated into a dog's eye, very marked keratitis results, in which spirochaetes are found in fairly large numbers. This predilection of the organism of syphilis for the cornea merits particular attention, for inoculation into all other parts of the body of mammalia, except in monkeys, is usually without any effect.

All the preceding facts as to the presence of Schaudinn's spirillum in every kind of acquired syphilitic lesion, as well as in hereditary syphilis and in experimental syphilis, cannot but form, when taken together, proofs of the very greatest importance in favour of the aetiological part played by this organism.

CHAPTER VIII

TOPOGRAPHY OF THE *SPIROCHAETE PALLIDA*; ITS CONNEXION WITH THE CELLS OF ITS HOST

From the time when it was found possible to find the *Spirochaete pallida* in sections, we have been able to study the problems of its connexions with the cells of its host with considerable accuracy. Thus it has been shown most clearly that a certain number of the spirilla pass into the blood, shortly after the appearance of the primary sore, while others are to be found in the lymph; these facts were proved by Burnet and Vincent[53] and by Levaditi[54] in their first researches on the spirillum, in experimental chancres in monkeys.

The organism appears, however, to have a much greater preference for the blood-vessels and lymphatics; for in a very large number of cases the organisms have been found in the actual walls of the vessels themselves. In every sort of syphilitic lesion they have been found in the parts surrounding the vessels; here they often form a dense network.

Although they are rarely found in the superficial parts of a chancre, they are especially to be seen in the deeper parts of the epithelial layer of the skin, where they are to be found in the intercellular, as well as in the interfibrillary spaces. Very often they can be traced into the connective tissue, where they very curiously imitate the form and undulations of the wavy bundles of connective tissue fibrillae. All these facts, already well established, form an important link in the chain of the aetiology of syphilis.

A very general fact, although it is not without exceptions, is the simultaneous appearance of syphilitic spirilla together with the mononuclear leucocytes which are so characteristic of syphilis.

For a long time the lesions have been well known. Where, as a result of this affection, there is found an abundant infiltration, in which we certainly do find polynuclear leucocytes, but in by no means such great numbers as that of the mononuclear elements which have often been described under the somewhat vague name of 'embryonic cells', those so-called 'plasmatic cells' would often appear to have an important relation to them.

As a general rule, whenever these changes are observed in a case of syphilis, we find at the same time spirilla. In those places only, where these organisms are particularly heaped up together, the mononuclear elements would seem to be much less in number than in the neighbouring parts, or else the wandering cells are much more numerous than the spirilla.

These facts may be interpreted in the following way. The spirilla produce some substance which promotes on the part of the leucocytes in general, and the mononuclears and other macrophages in particular, a chemio-taxis or positive sensibility; these cells are then directed towards the parts invaded by the micro-organisms; after this there is an actual contest between these two living elements. The organism puts into activity all possible means to maintain itself as well as to reproduce itself in the infected host, whilst the latter raises its army of defence to destroy the parasite as far as possible.

There were not sufficient facts to be able to judge of the intricate phenomena which take place in syphilis until after the revolution in syphilography which was brought about by the discovery of Schaudinn's spirilla in experimental syphilis. But a short time before this new discovery in science, Dr. Nagelschmidt[55] published a work on the immunity of syphilis, in which he affirmed that phagocytes certainly take no part at all in the defence of the organism against syphilis. After this, many observers have studied this problem, and their results show clearly that Nagelschmidt was by no means a true prophet.

Ehrmann,[56] a well-known syphilographer, has written the most complete work on this question. He worked on indurated chancres and primary lesions, inoculated living subjects, and studied under the best possible conditions. We add the conclusions which this observer came to in his last work: 'The spirochaetes first penetrate into the interstices of the tissues, and after that reach the blood and lymphatic vessels' (p. 240). 'The development of the capillaries, in just the same way as the migration of the leucocytes, we must regard as a phenomenon which depends on a chemio-tactic irritability. The leucocytes, which have passed right through the wall of the new-formed capillaries, now pass into the interstices of the tissues of the lymphatic ducts. Here they produce leucocytic infarcts, and these later on show all the stages of phagocytosis. This proves that the leucocytes form some means of protection against the propagation of the virus.' 'In the Tunica intima of the lymphatic vessels, the spirochaetes, which have come from without, cause the same changes as in the connective tissue; that is to say, increase in size and direct division of the fibroblasts, thus causing a thickening of the Tunica intima and the formation of new capillaries. These hypertrophied fibroblasts have exactly the same phagocytic action on the spirochaetes as that of the rest of the connective tissue, and by their proliferation they can bring about in a short time a more or less complete obliteration of the lymphatic vessels' (p. 241).

In secondary lesions Ehrmann has been able to show spirilla enclosed in phagocytes. The phagocyte has been shown within papules in the stage of weakness of the general pathological process; and it has been found to be abundant in the skin, more especially in macular syphilides.

Later, Ehrmann expressed the opinion that in phagocytosis we have one of the opposing forces of the organism against spirochaetes. 'The infiltration is part of this phenomenon like the formation of the leucocytic infarcts in the smallest lymphatic channels, for these parasites are also found among phagocytic elements. Perhaps even the malignity of syphilis in cachetic persons depends on the feeble power of their white cells' (p. 243).

The fact that phagocytosis has not been found in some cases of syphilis depends, according to Ehrmann, rather on the still imperfect state of our methods of research than upon their actual absence. Thus, 'In two fragments coming from one and the same chancre, which were stained at different times, although the staining did not show spirochaetes, phagocytosis was only shown in one of these cases, although the spirochaetes were large in number and well marked in appearance in both ' (note on p. 243).

This is perhaps the reason why many workers, amongst whom I can quote most able observers, such as Levaditi and Manouélian, failed in their attempts to find phagocytosis in primary and secondary syphilitic lesions. On the other hand, the former of these observers was quite certain that he had seen the engulfing of spirochaetes by phagocytes in hereditary syphilis. Levaditi [57] was struck when examining a case of pneumonic consolidation in a congenitally syphilitic child who died shortly after the mother's delivery, by the quantity of macrophages found in the pulmonary alveoli which contained spirilla. ' Here we have to do with the true phagocytic phenomenon followed by the digestion of the elements of the spirilla in the protoplasm of these macrophages,' —to quote again from the author,—' the proof that alterations are undergone by the spirilla when enclosed in this protoplasm is to be found in their varicose appearance and transformation into granules ' (p. 66).

Amongst observers who have found *Spirochaete pallida* within phagocytes in cases of acquired syphilis I may quote Schaudinn himself,[58] who has seen them in the interior of a mononuclear corpuscle contained in a blood-vessel taken from a secondary papule in man.

The phagocytosis of syphilitic spirilla has been recently described by Gierke,[59] in a child who died four days after its birth. The organs were found healthy at the autopsy except the lung, which contained a yellowish-white focus of disease due to hereditary syphilitic pneumonia. In sections large quantities of spirochaetes were found. These were surrounded by leucocytes which had accumulated together in abundance, and were very often lodged in the actual interior of the cells. A more detailed examination showed that these cells were sometimes mononuclears though the polynuclears contained the organism much more frequently ' (p. 351). Some of them only contained one or two spirilla, whilst others contained large masses of them.

In the preparations of Levaditi and Gierke, which I have examined myself, I had no difficulty in being convinced of the accuracy of their statements (Plate VIII, *a*). The existence of phagocytes in syphilis therefore cannot be really called into question. This is quite in accordance with the way the principal pathological processes have been interpreted: these have been so well studied in the case of syphilis long before Schaudinn's discovery.

But although the presence of spirilla in the white cells is only a repetition of the phenomena of phagocytosis, so well known in other infectious diseases and now established in the case of syphilis, certain facts would appear to lead us in a new direction. While examining sections from the organs of hereditary syphilis in children, Levaditi seems satisfied that very often the spirilla are to be found contained in other varieties of cells, which have nothing to do with the white corpuscles nor with any other kind of phagocytes. 'We have to conclude', says this author, 'that the spirilla of syphilis have the power of penetrating into the relatively intact protoplasm of certain epithelial cells, such as those of the liver and of the kidneys, the cells of the suprarenal capsules, and probably also those of the sweat glands' (loc. cit., p. 63). These facts have been confirmed by several observers, and can no longer be doubted.

The only difficulty that remains is to interpret this fact. As Levaditi remarks, 'we still have to determine whether the intra-protoplasmic existence of the parasites is due to their active penetration into these cells, the cells retaining all their vitality, or whether there is in this, something of an agonic phenomenon, whose cause is, so to say, the state of inertia in which these cells are during the few hours which precede death' (loc. cit., p. 63).

It is to be noted in this connexion, that in preparations taken from tissues removed during life, as in the researches of Ehrmann, which we have already quoted, the spirilla were only found in the interior of true phagocytes, and they have never been seen in the epithelial cells such as those of the skin or sweat glands.

On the other hand, demonstrations of spirilla in the interior of epithelial or other glandular cells have only been made from organs which have been removed after death. It is true that in one case Levaditi was able to examine the tissues of a child very soon after death, at a time when the spirilla were still living, and in spite of this he found them in the interior of the epithelial cells, but of course it was quite possible that these cells had died before the death of the microbes.

The problem therefore cannot be very definitely settled. Gierke thinks there may be an actual phagocytosis of glandular cells, calling attention to the researches of Rössle on the phagocytosis of red cells by the epithelial cells of the liver, kidney, and pancreas. As the *Spirochaete pallida* is to be found in certain internal organs of monkeys, such as the testicle, it is in this direction we must look for the problem of its presence in those elements which usually have no phagocytic action. This subject is to be recommended for future research.

As syphilis is a malady which can undergo spontaneous cure, and which is nearly always very amenable to proper treatment, it ought to be very interesting to find out the ways by which a cure is effected. For this research monkeys should provide a good field, as in them syphilis is cured spontaneously in all but a few rare cases.

Levaditi has undertaken some work on this point; he has satisfied himself that the spirilla persist for a long time in primary sores, even when these appear to be completely healed. Many other observers have followed the life-history of the spirilla in human syphilis, when treated by mercury. Some have been struck by the long persistence of these organisms even when the cure seems to be quite perfect. Thus Galli, Valeris, and Lassueur[60] found a large number in an ulcerated papule which was nearly healed, and even after twenty centigrammes of sublimate had been injected. Levaditi and Sauvage[61] have found *Spirochaete pallida* in the blood and organs of a syphilitic infant whose mother had been treated with biniodide of mercury and iodide of potassium from the second month up to the end of her pregnancy.

On the other hand, some workers, among them Lévy-Bing,[62] have found that the spirilla disappear after mercurial treatment. The cause of the disappearance of these organisms has not been settled, and it is quite possible that the action of mercury is towards strengthening the defences of the body rather than any direct lethal action on the spirochaetes themselves. With regard to the therapeutical action of atoxyl in syphilitic lesions, a fact that cannot be denied, the work of several observers has indicated that this substance does not kill the germs, but exerts its influence in strengthening the phagocytic defences of the host. This is also the opinion of Uhlenhut.[63]

CHAPTER IX

NATURAL HISTORY OF THE MICRO-ORGANISM OF SYPHILIS

The study of Schaudinn's spirillum in syphilis, together with the recognition of its constant presence in syphilitic lesions and its reappearance in an infected host are facts of the greatest importance in dealing with the great weight which should be attached to the presence of the organism. It is, however, desirable, in order to be able to form a conclusive judgement on this subject, first of all to know something about the natural history of the spirillum as well as its relations to the other micro-organisms which appear in a spirillar form.

We have already detailed in the second chapter (chapter VI) the very important part played in this question by the differentiation of the *Spirochaete pallida* from the other spirilla which are found in syphilitic lesions in man.

The following would appear to be the characteristics of the *Spirochaete pallida,* according to the work published by Hartmann and Prowazck, from writing found after Schaudinn's death.[64] In length it averages 6–15 μ, although some specimens are longer than this and measure between 16–26 μ. Its transverse measurement is so minute than it can hardly admit of measurement; it is about $\frac{3}{4}$ μ. Its undulations are extremely characteristic, especially as they remain the same during rest as well as in movement; this is what Schaudinn remarks himself: 'In comparative research we find at the very start that the *Spirochaete pallida,* which is only found in syphilitic lesions, varies extremely little in appearance; quite unlike the other known varieties of spirochaetes. As soon as one has had any experience, it is extremely easy to distinguish it from other forms when it is in the living state. The delicate shape and slight refractive power of *Spirochaete pallida*, together with its typical spiral form with very numerous undulations (10–26), all perfectly regular, well marked and closely resembling each other, make it very difficult to mistake it for any other object whatever.

'The following fact is of particular importance, and is to be observed when examining the living organism—it is that the typical spiral form is to be seen not only when it is actively moving, but also when it is at rest; whilst all other analogous spirochaetes which present marked undulations show these only when they are moving vigorously, and when at rest have long flattened-out undulations, and indeed are very nearly straight. This particularly "stiff" appearance—so to speak—in *Spirochaete pallida* is due to the fact that in it the spiral arrangement seems to be definitely formed, and does not shift in any condition, whilst in other varieties the deep spiral is only produced during rapid movements and is straightened out at rest. There is only one spirillum, that of the mouth or *Spirochaete dentium*, which has a smaller fixed spiral arrangement, but this variety can be distinguished by other characteristics from the organism of syphilis.' 'The undulatory membrane has not yet been demonstrated in *Spirochaete pallida*.' 'At the present time I am inclined to think that the body of *Spirochaete pallida* may be round in section, that is to say, that the organism is cylindrical and not flattened as other spirochaetes are when observed from this point of view.'

The peripheral part (periplasium) is of equal thickness in the whole organism. It thins out at both poles and is continued in the form of a cilium whose length equals that of from four to six undulations. Schaudinn, at the end of his work, was able to recognize these cilia much better in the living organism than in stained preparations.

The largest individuals are distinguished by the presence of two cilia at one pole of the spirochaete. Schaudinn was able to confirm his speculation, that this was the beginning of a longitudinal division. These are his words concerning this in a report given in December, 1905: 'Owing to my somewhat long experience in this connexion, I am now able to recognize vibratile cilia in the living organisms at each pole of the spirillum, but, and this is still more important, I have already succeeded in three cases in observing the longitudinal division of the organism. To follow out this process I have chosen individuals which already possessed two fine cilia at one of the poles, and I have seen longitudinal division progressing in a very few seconds beginning at this pole. At the moment of division, the organism abandons its marked spiral form and appears to be very irregularly contorted.'

All these details should be sufficient not only to distinguish the spirillum of syphilis from all related varieties, but also to give us some idea of its place among micro-organisms generally.

Here we touch on a problem which is very much debated in microbiology, as well as a subject where opinions are far from being unanimous. From the first observations on spirilla up to quite recently, these organisms were unanimously considered as belonging to the group of bacteria. In the attempts at classification made by Ehrenberg (1838), and Cohn (1875),[65] the spirilla were placed with the bacilli. The latter of these two great experts in microscopical organisms divided those bacteria which had a spiral arrangement into three classes :—

1. *Vibrio*, consisting of those microbes with a very simple spiral.
2. *Spirillum*, rigid and rolled in the shape of a corkscrew.
3. *Spirochaete*, a spiral organism with a flexible body.

The last class embraced the *Spirochaete plicatilis*, *Spirochaete denticola*, and *Spirochaete Obermeieri* of recurrent fever.

This distinction could not be maintained for any length of time, for amongst the bacteria there were some which, in a single species, contained the characteristics of the three varieties of Cohn.

Thus, for example, the organism of cholera is well known, owing to the great ease with which it can be cultivated. Now we find that it is usually seen in the form of a vibrio with a very simple curve (Plate VIII). On the other hand, under certain particular conditions it appears as a spiral filament, with either a simple or else a corkscrew curve. When these spiral filaments are short the body and organism show no signs of flexibility;

but when they are very long they undergo the very flexible movements of a spirochaete (Plate VIII, *c*).

We have another example in the organism of recurrent fever; this, under ordinary conditions—that is to say, when it is found in the blood of patients during the attacks of fever—appears as a true spirochaete with a flexible body. But in patients who have malarial parasites in their system at the same time that they are suffering from recurrent fever, the spirillum of Obermeier, as has been shown by Karlinsky,[66] is divided into bodies which resemble much more closely the vibrios of cholera than any form of spirochaete.

More recently, Migula[67] has endeavoured to place the classification of spiral organisms on a more complete basis. For this he divides them into four varieties :—

1. *Spirosoma*, spiral organisms, immobile and without cilia.
2. *Vibrio*, comprising short vibrios curved on themselves and showing one, two, or even more than three cilia at their extremities.
3. *Spirillum*, micro-organisms of a spiral helicoid form provided at each end with several cilia.
4. *Spirochaetes*, very long *Spirilla* with more or less numerous and regular undulations and without cilia. Some of these spirochaetes have an undulatory membrane closely analogous to that of trypanosomes (*Sp. plicatilis*, Ehrenberg).

It is easy to see that this classification, which is really very little different from Cohn's, has indeed no foundation on fact. The organism of cholera would have to be classed among the vibrios when its numbers are small; at other times under *Spirillum* or *Spirochaete*. The true *Spirochaetes*, as, for example, those which cause septicaemia in fowls, or tick fever in men, seeing that they possess numerous cilia, should be excluded from this class altogether, as far as Migula's classification goes.

The latest modification proposed by Swellengrebel[68] has no better chance of success; he divides Migula's *Spirillaceae* into two sub-groups :—

1. *Spirillaceae*, whose bodies are not flexible, composed of

the genus *Spirillum* and *Vibrio*; and *Spirochaetaceae*, whose bodies are flexible, this class containing three sub-classes:

(1) *Spirochaete.*
(2) *Treponema* or *Spironema* (organism of syphilis).
(3) *Borrelia* (organism of septicaemia in fowls).

Unfortunately, in this classification again, no account has been taken of the vibrio of cholera, which is found at times in the form of long spiral flexible filaments.

The failure of all these attempts to classify spirilla is due to the very imperfect knowledge we really possess with regard to these organisms. I believe, therefore, under present conditions, that it is quite beyond our power to endeavour to imprison the few spirillar organisms which we now know within the very narrow limits of precise classification. Rather, at a later date, this should be the crowning-point of profound and extended study of the entire group.

It is on account of the imperfect state of our present knowledge that I have attached no great importance to the mere names proposed by different authors, and have purposely called the various spiral micro-organisms by the one name of *Spirilla.*

In the attempt to increase the sum of our precise knowledge of this microscopical world of its own, Schaudinn, whose loss we must ever deplore, was able to gather together a great number of new facts concerning it. In the course of his researches for parasites in the blood of certain birds,[69] he was struck by the fact that certain trypanosomes, or small flagellated protozoa, produced spiral enrolled filaments, each one resembling spirochaetes (Plate VIII, *d*). These were very minute organisms provided with an undulant membrane, which is very characteristic of true trypanosomes, and, like them, they were reproduced by longitudinal division. This discovery suggested to the distinguished author the idea that many spiral organisms, hitherto taken for bacteria, more especially the different spirochaetes of recurrent fever, septicaemia in birds, &c., were nothing less than very fine trypanosomes, and thus were flagellated infusoria, and not bacteria at all.

Working on this hypothesis, Schaudinn set himself to seek for the true spirochaetes, and selected the study of *Spirochaete Obermeieri* of recurrent fever. It would seem that the facts which he collected on this subject were not very favourable to this theory. Nevertheless, his researches familiarized him very considerably with the world of spirilla. This was a fortunate circumstance, as he was thus able to recognize the spirilla in syphilitic products, when so many other observers had failed. If Bordet and Gengou had possessed the same skill and experience in observing spirilla, they would probably have found them in the preparations from chancres which appeared to them to be absolutely devoid of organisms.

When the discovery by Schaudinn of the organism of syphilis had attracted general attention, this able protozoologist set himself to follow out his idea as to the position of these spirals in the general system of micro-organisms.

We must remember that at the beginning of his task he was already very skilled in the identification of trypanosomes and spirochaetes. In an article[70] full of valuable suggestions, he expressed the opinion that very small trypanosomes, rolled in a spiral, had no very near genealogical connexions with the true spirochaetes (such as *Sp. plicatilis* and *Sp. Obermeieri*), and that, in consequence, any attempt to discover in them all the characteristics of trypanosomes was useless.

In the work published in Schaudinn's name after his death by Hartmann and Prowazck,[71] we find his opinion thus expressed on the question which is now occupying us: 'I must confess', says this lamented scientist, 'that the question of the place they occupy in the system of nature has but the smallest scientific interest. For a long time I have been convinced that bacteria and protozoa do not form two separate and distinct trunks, but are really two branches from the same tree, that of the unicellular organisms or "protista"; and that these two branches have many side connexions. However, scientific study in this domain may teach us to find one of these stages of transition among the spirochaetes, which may well lie between the flagellated organisms and the true spirilla which are reproduced by transverse division' (p. 16).

It appears to me that some observers in the pursuit of Schaudinn's original conception have gone very much further than the author himself. Schaudinn's successor in the Institute of Hamburg, Prowazck, attempts in many recent publications to prove that spirochaetes in general, are indeed trypanosomes or their nearest relations. In his argument a very important part is attributed to the longitudinal division which is typical in trypanosomes, but is believed to be absent in bacteria: so careful an observer of micro-organisms as Schaudinn has insisted that 'Longitudinal division is a process which is characteristic of flagellates, and up to the present has not been proved in any one bacterium. The latter always divide transversely' (Posthum. note, loc. cit., p. 16).

Nevertheless, it is well known that a great number of micrococci divide in two lines, perpendicular one to the other; some sarcinae even divide in three directions, but in the elongated forms there are undoubtedly some which undergo longitudinal division.

I myself described a bacterium in 1888[72] which I called *Pasteuria ramosa*, oval in shape, which divided longitudinally. It is true that Migula[73] has refused to believe that *Pasteuria* is a bacterium at all, although in this he is most assuredly wrong, because the production of spores shows clearly the bacterial nature of this organism. We cannot deny in some other cases that bacteria are really able to divide longitudinally.

Following the same suggestion of the connexion of spirochaetes with trypanosomes, Prowazck[74] affirms that the spirillum of septicaemia in fowls (*Spirochaete gallinarum*) divides longitudinally, contrary to the observations of other observers, amongst whom I may quote Levaditi.[75] The description of the division in Prowazck's papers, and also the pictures meant to illustrate it, are very far from being convincing.

On the other hand, the researches of Koch,[76] and Zettnow,[77] carried out with the greatest care, show clearly that the spirochaete of tick fever, which so closely resembles that of fowls, is reproduced by transverse division. The photographs in Zettnow's account, moreover, form a convincing argument. I may add that, in the course of my own research on the *Spirochaete Obermeieri* and the organism of septicaemia in geese, I was able to find transverse division of these organisms without seeing the slightest indication of longitudinal division.

In a recent paper on spiral organisms found in the oyster, Borrel and Cernovodeanu [78] affirm categorically that this *Spirochaete Balbiani* (Plate IX, *b*) divides transversely, and yet here we have to do with an organism which approaches very closely to the flagellates, and which, for this reason, has often been taken for a trypanosome.

In a recent article, already quoted, Swellengrebel decided in favour of transverse division, not only of the parasite of the oyster but also of the *Spirochaete buccalis* (loc. cit., p. 580). Hartmann and Muhlens [79] have succeeded in cultivating *Spirochaete dentium*, and have given many details concerning its reproduction. But although they were then able, without difficulty, to observe transverse division, it was but rarely that they came across any stages which perhaps might be part of a process of longitudinal division. The authors themselves, however, make no final statement on this point.

Under these conditions it is quite clear that the whole question must be studied afresh, and that, despite the statements of Schaudinn, of Krzyztalowicz and Siedlecki,[80] and of Herxheimer,[81] the existence of longitudinal division in spirochaetes in general and in the *Spirochaete pallida* in particular, must be proved afresh by most certain and convincing arguments.

The study of the organs of locomotion of these organisms presents a second point which is a subject of much discussion. The bacteria move by means of cilia, whilst the organ of locomotion in trypanosomes is an undulant membrane. If the micro-organism of syphilis is a bacterium it ought to possess cilia ; but if, on the other hand, it belongs to the group of trypanosomes, we ought to find that it possesses an undulant membrane. In his first work Schaudinn, being rather inclined to associate spirochaetes with protozoa, believed that he had seen an undulant membrane in *Spirochaete pallida*, but at a later period, as I have already mentioned, he had to modify this opinion after having proved the existence in these organisms of two cilia at the opposite poles of the body. In spite of his observations, partizans of the theory that spirochaetes are flagellated infusoria endeavour to show the presence in them of an undulant membrane. Thus Prowazck (loc. cit., p. 559) admits the presence of this membrane in the spirochaete of fowls, and this despite the discovery by Borrel[82] of vibratile cilia round the body of this organism (Plate IX, *a*, *Spirochaete gallinarum*, with vibratile cilia, after Borrel). Zettnow[83] was able to confirm this same fact by studying the connexion of this organism with the spirochaete of African tick fever.

It would thus seem to be proved that certain spirochaetes are indeed in possession of a true undulant membrane. During the last few years Schaudinn has described them in *Spirochaete refringens* and *Spirochaete plicatilis*; Hoffmann and Prowazck,[84] have seen the same in *Spirochaete buccalis*; Borrel and Mlle. Cernovodeanu (loc. cit.) have studied it in detail in *Spirochaete Balbiani* of an oyster (Plate IX, *b*, *Spirochaete Balbiani*, after Borrel). This curious organism, by its transverse division is closely connected with true spirilla, yet by its means of locomotion recalls the trypanosomes.

We cannot fail to see by all these facts that the discussion as to the place which the micro-organism of syphilis should take in the classification of organisms in general has brought about the discovery of a certain number of very important facts, and, although they are, up to the present, insufficient to deal definitely with the question, they have contributed most important results.

The more detailed knowledge of spirochaetes allows us to affirm with certainty that the spirillum of Schaudinn is a species quite distinct from the *Spirochaete refringens* and *Spirochaete balanitidis*, which have been found in certain syphilitic lesions and have been called secondary organisms.

This conclusion alone is quite important enough to console us for the impossibility up to the present time of obtaining a precise knowledge of the relations of the organism of syphilis to the other members of the legions of micro-organisms.

The *Spirochaete pallida* would appear to be an exceedingly delicate micro-organism which perishes very rapidly in the absence of moisture, and even in the presence of moisture it is only kept alive with great difficulty. It is true that Hoffmann[85] has kept it in a motile condition for several weeks; on the other hand, it has been fully established by other researches that the virus of syphilis retains its pathogenic power outside the body for a few hours only, while Landsteiner and Mucha[86] have been able to keep the organism alive only for two days at the very most.

All attempts to establish the cycle of development in *Spirochaete pallida* have, up to the present, led to no satisfactory result. Krzyztalowicz and Siedlecki, in the memoir which we have already quoted (p. 82), have described a whole series of different forms which they believed to be stages in the development of the organism of syphilis. They observed very large spirilla which they recognized as macrogametes, or female elements, capable of sexual reproduction. They observed their union with very small spirilla which they took for the male elements. If this be correct the reproduction of *Spirochaete pallida* would closely resemble that of the protozoa.

Unfortunately the research of these Polish authors was effected by working with syphilitic lesions which were already of long duration, and therefore could not be considered to be free from contamination with organisms other than that of syphilis. Having in view the very great difficulty of this kind of observation, we must wait for results which will confirm these authors' work. This would seem to be all the more necessary, as in hereditary syphilis, where the organs are invaded by an enormous number of spirochaetes without being contaminated by any other organism, no one has yet found the particular stages described by the Polish observers.

Seeing the important part which this organism would appear to take in the aetiology of syphilis, it is clearly of great importance to be able to cultivate it in artificial media. Attempts to do this have been made in nearly every bacteriological laboratory in the world, yet up to the present none have been successful. Having regard to the great difficulty of obtaining anything like a proper quantity of Schaudinn's spirillum in a pure state with which to sow media, some observers have worked with other varieties of spirochaetes as closely as possible allied to that of syphilis. Working on these lines, Muhlens[87] has obtained pure cultures of *Spirochaete dentium*, which appear to grow well, under anaerobic conditions, in serum agar. Levaditi,[88] on his part, has been able to make luxuriant cultivations of the spirillum of African tick fever, of the spirillum of fowls, and of the *Spirochaete refringens* by means of bags of collodion, placed in the peritoneal cavity of rabbits. In these cultures he has watched the development of several generations without observing the occurrence of any trypanosomic form. These results give reason to hope that the organism of syphilis may be cultivated at no distant date.

We may well conclude this chapter by adding a few words as to the actual name given to the organism of syphilis. Schaudinn, after having first given it the name of *Spirochaete pallida*, joined later on with Vuillemin in renaming it *Spironema pallidum*; however, after he had found that the name of Spironema had already been made use of to describe another kind of micro-organism, Schaudinn invented a new name *Treponema pallidum*. At the same time, however, Hoffmann—whose collaboration with Schaudinn had been already of such great value in the progress of our knowledge on this organism—abandoned this name, and used that of *Spirochaete pallida* or *Spirochaete pallidum*. I shall follow the example of this German syphilographer, as I consider that the time is still premature to make any classification of spirillar micro-organisms.

CHAPTER X

TECHNICAL METHODS IN CONNEXION WITH THE ORGANISM OF SYPHILIS

As we have already seen, the organism of syphilis was first discovered in a living state in a fresh preparation from a syphilitic lesion. This method, simple as it is, must be seen to have a much greater importance than all the complicated processes employed many hundreds of times before Schaudinn. It must, however, be said that examination in a fresh state is by no means easy, more especially in those cases (and these form the majority) where the organism exists in very small numbers. To be successful a very favourable light is necessary. I only succeeded in observing them when using a gas lamp with an Auer shade, although in the same preparation, when observed with the same lenses, but using daylight or an ordinary electric light, I was unable to see a single pale spirillum. In the presence of these difficulties we must regard the discovery of a simple and precise method of looking for the organism in fresh preparations as a great advance in our knowledge. Landsteiner and Mucha (loc. cit.) have done this. These observers have applied the principle of the ultra-microscope of Siedentopf and Zsigmondy for the examination of small particles in a dark field. To do this they used a condenser made by Reichert, of Vienna, which would appear to be the best of these instruments. The illumination is given by an arc lamp of 20 ampères. The most satisfactory combination of lenses has been found to be that of a dry objective, No. 5, with Reichert's compensatory ocular, No. 18. An examination is made by taking a small amount of syphilitic secretion, which is then rubbed between cover slips into a film; the cover glasses protect it against desiccation. In those cases where the material contains too many solid particles it is treated with normal saline solution; in these conditions the syphilitic spirilla are seen on a dark background between all sorts of corpuscles, in the form of motile organisms, strongly illuminated and easily recognizable (Plate X, *b* and *c*). The extraordinary mobility, combined with the spiral appearance, enables us very readily to distinguish the spirochaete of syphilis from other spirillar organisms. Usually an examination of a few minutes is enough to confirm our diagnosis. This very interesting and convenient method, which has already been confirmed by Hoffmann and other specialists, may now be considered as a necessary part of daily practice.

Thanks to the ease with which we are now able to recognize the organism of syphilis with a dark background, methods of staining syphilitic products in film preparations have been recently relegated to a second place. Nevertheless, their importance remains, not only in observing the minute anatomy of the spirilla, but also in all those cases where we desire to keep preparations for some time. Before staining the films, in each case we have, of course, to obtain the necessary material for their preparation.

As has already been shown many times, the *Spirochaete pallida* is much more abundant in the deeper parts of syphilitic lesions, whilst on the surface its number is very small. Sometimes they are not found at all in the peripheral parts of the lesion. This peripheral part is, on the other hand, very often the seat of secondary organisms, amongst which we may meet the *Spirochaete refringens* together with bacilli and micrococci. For this reason we should as far as possible take material from the deeper parts of syphilitic lesions in order to make film preparations.

Sometimes it is useful, in connexion with syphilitic lesions of the skin, and even with portions of healthy skin in the immediate neighbourhood of these lesions, to use *vesicants* after the methods of Levaditi and Petresco.[89] After the surface of the skin is washed, a vesicant is applied either on the lesion or on the neighbouring parts, over a surface of about two square centimetres; this is left in position for from six to eight hours. The liquid which accumulates can now be removed by a sterile pipette introduced under the skin. Again, the vesicle may be excised and the bare surface thoroughly rubbed: the serum which exudes will serve for other film preparations.

In the study of *tertiary lesions*, material must be removed from the peripheral parts and not from the mass of the caseous gumma itself. With regard to the vesicles of pemphigus in new-born children and the pustular eruptions in adults, the contents should be removed for making film preparations.

The best method of finding the spirilla of syphilis in the *blood* is that of Noeggerath and Stoehelin.[90] The blood of the ear is taken, or, better still, one of the veins of the arm is punctured, and diluted with ten times its volume of a solution of acetic acid of one in a thousand. At least 1 c.c. of blood must be removed. The blood diluted in this way should be thoroughly centrifugalized, after which it can be used to make film preparations.

It is often very important to make a microscopic examination of the juice of glands; this should be removed from the living subject. For this purpose, as Hoffmann has shown, the inguinal region must first be shaved, then disinfected and washed with saline solution. After this the sharp needle of a syringe, holding 5 c.c., is introduced into the inguinal gland, which is fixed in position by the left hand. We should endeavour to pierce one of the largest of the glands and remove its contents by slow aspiration. If the gland follows the movement of the needle it proves that the needle is actually in the interior of the gland. After a sufficient quantity of the juice of the gland has been taken away, the syringe is emptied on to a clean plate and the film preparations are made with fine layers of the extracted fluid.

In taking material from an autopsy, the technique is so simple that there is no need for any further explanation.

The films obtained by these methods should be stained by one of the methods which have been found best in studying the organism of syphilis. Giemsa's method is the one which, undoubtedly, takes the first place amongst these methods of staining. The films are fixed in strong alcohol and then treated for one or several hours with a mixture composed of a solution of azure blue and eosine. Giemsa's mixture, ready prepared, can be easily bought.* Fifteen drops of this solution are taken and mixed with 10 c.c. of distilled water. The spirilla of syphilis are feebly stained by this method, and usually show a clear rose colour, whilst the other spirilla, especially *Spirochaete refringens*, are coloured violet. We should, however, mention that this staining is not sufficiently constant to allow us to use it to differentiate the microbe of syphilis from others.

Instead of fixing the films by alcohol, Hoffmann and Halle advise another method. They put in a flat plate 5 c.c. of a one per cent. solution of osmic acid, and add to it ten drops of glacial acetic acid. The films are then exposed for at least two minutes to the mixed osmic and acetic vapours. For this method the syphilitic products are rapidly spread out on to slides which have been exposed to the osmic acid vapour, and before the films are dried they are again exposed to the same vapour for one or two minutes. The films, being thus fixed, are now treated for about a minute with a very weak solution of permanganate of potash, washed in water, dried, and finally stained.

The osmic acid may be without inconvenience replaced by formalin.[91]

Instead of staining by Giemsa's method as explained above, one of the following methods may be used:—

Giemsa's New Method.[92] As soon as the material is obtained, it is treated with a freshly made mixture, obtained by adding 5 to 10 drops of a solution of carbonate of potash of 1 in 1,000 to 10 c.c. of distilled water. While the liquid is being constantly shaken, 10 drops of Giemsa's commercial stain are added to it. With this method it is found sufficient to leave the slides in the staining bath for from three quarters of an hour to an hour. Herxheimer[93] has proposed to stain the films when fixed with alcohol with a hot solution of gentian violet. A quarter of an hour is enough to obtain a good staining of spirilla. By heating the preparations

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* Giemsa's latest formula is the following:

Azur ii, Eosin	3	grms.
Azur ii	8	,,
Glycerine (Merck, chemically pure) .	250	,,
Methyl alcohol (Kahlbaum i) . . .	250	,,

these organisms can even be sufficiently stained in half a minute. Preis[94] has further modified Giemsa's method for films of syphilitic products; these are thrown on to a mixture of 20 to 25 drops of Giemsa's stain diluted by 10 c.c. of distilled water. The plates are then kept about 5 cm. above a Bunsen's flame and heated until vapour comes from them, taking care that the liquid does not boil. The same process is repeated twice, and in five minutes the preparations are finished; in them the organisms of syphilis are stained quite a *deep red.*

Marino's method[95] is also distinguished by its rapidity. The films are first dried without being fixed in any way, and then are treated by a mixture of Marino's blue (0·1), and of methyl alcohol (20·0). After three minutes some drops of a watery solution of eosin (0·05 in 1,000) are added. Two minutes after this the films are thoroughly washed and are now ready to be examined. I have myself found this method of the greatest use.

In order to stain the terminal cilia of *Spirochaete pallida*, *Loeffler's method* should be used. A freshly made mixture is used, consisting of—

10 c.c. of a 20 per cent. solution of tannin;
5 c.c. of a cold saturated solution of sulphate of iron;
1 c.c. of a saturated alcoholic solution of fuchsin.

This mixture is put on the film, and the whole is heated three times until vapour comes off. It is then washed in distilled water and stained with Ziehl's solution of carbol-fuchsin, gently heating it at the same time. By this means the organism of syphilis is stained a dark red, whilst its cilia are shown in a light rose colour. Care must be taken in all these methods to dilute the syphilitic products with some drops of distilled water.

Many other methods have been proposed for the staining of films; but those which we have shown are quite enough to obtain good preparations of Schaudinn's spirilla.*

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* Plate XIII shows a film preparation stained by Leishman's 'serum method', which may be briefly described: The film is fixed in methyl alcohol for half a minute, this is blotted off with cigarette paper and a thin layer of fresh blood serum is run over the surface of the film. Only a single drop of serum is required, and this is drawn over the surface of the film with a needle. The excess is then removed by allowing the slide to stand on one end, and the film is

Formerly the greatest difficulty was found in obtaining a proper staining of various spirochaetes in sections, and only a very partial effect was obtained in the case of the organisms both of recurrent fever and of septicaemia in geese and fowls. But since the study of the organism of syphilis first attracted the attention of a great number of workers, an extraordinary amount of progress has been made in this branch of micro-biological technique.

Bertarelli and Volpino,[96] were the first to apply Van Ermenghem's method of staining cilia to syphilitic tissues. Their sections are treated from 24 to 48 hours with a solution of nitrate of silver (0·2 to 0·5 per cent.). After washing it rapidly with distilled water, it is then treated for a quarter of an hour with Van Ermenghem's solution, which is composed of—

5·0 acid gallic.
3·0 tannin.
10·0 acetate of soda.
350·0 of distilled water.

The sections, as soon as they are stained yellow in this solution, are again placed in the nitrate of silver solution until they are stained brown; after being again washed in distilled water they are passed in the usual way through alcohol and xylol, and finally mounted in Canada balsam.

After some time Bertarelli and Volpino[97] modified their original method and perfected it in the following way: Very thin sections (not more than 7 μ in thickness) are first fixed in alcohol, and then put into a bath composed of—

3 gr. nitrate of silver.
50 c.c. of alcohol (96 per cent.).
50 c.c. of distilled water.
4 or 5 drops of pure acetic acid.

The whole is put in a deep glass and gently heated between 35° and 37° C. (95°–98° F.) for three or four days. As soon as a precipitate is formed the fluid to be renewed. After repeated

then allowed to dry in the air. The film is now stained with a mixture of equal parts of Leishman's stain and distilled water. After twenty-five minutes the stain is washed off and the film dried and examined. The serum intensifies the action of the stain and prevents the occurrence of any deposit.—TRANSLATOR.

washing in distilled water the sections should remain in Van Ermenghem's reducing solution for 24 hours ; this is the same as that used in the last method. The sections are again washed with distilled water, and then dehydrated with alcohol in the usual way.

Whilst Bertarelli and Volpino's two methods are modifications of Van Ermenghem's method of staining cilia, Levaditi's method[98] is a modification, adapted for syphilis, of that of Ramon-y-Cajal for staining the terminations of nerve-cells.

Fragments of the tissue about 2 to 3 millimetres in thickness are fixed in 10 per cent. formalin solution for 24 hours ; they are then kept in 96 per cent. alcohol for the same time, then washed in distilled water until they fall to the bottom of the vessel containing them. They are then put into the following solution :—

1·5 to 3 grs. of nitrate of silver.
100 c.c. of distilled water.

The fragments are put with this solution into a wide-mouthed bottle with a tightly-ground glass stopper ; in this they should remain for three days in an incubator at a temperature of 38° C. (100° F.) *in the dark* : after this they are washed with distilled water and then put into the reducing liquid. This contains—

4 grams pyrogallic acid.
5 c.c. formalin.
100 c.c. distilled water.

The reduction is allowed to continue for 24 hours ; the fragments are now dehydrated, passed through xylol, and cut in paraffin. The sections (which should not be thinner than 5 μ) may be stained by Giemsa's method or by toluidine blue and neutral red, combined with methyl blue. This method should be that used by preference for staining spirilla in the organs of inherited syphilis. Many observers have already made use of it for all sorts of syphilitic tissues with the greatest success. (See Plates XIII to XVI.)

Levaditi, in conjunction with Manouélian,[99] has suggested another method, which they especially recommend for those tissues which are taken from the living body. Small pieces of tissues are fixed in formalin, 10 per cent. solution, from 24 to 48 hours, and then kept in 96 per cent. alcohol for 24 hours: they are then washed in distilled water and placed in the following solution:—

10 c.c. pyridine (added to silver solution at the moment of use).
90 c.c. of a 1 per cent. solution of nitrate of silver in distilled water.

They are kept in this solution, first at the temperature of the laboratory for two to three hours and afterwards from three to five hours at a temperature of from 45° to 50° C. (113–122° F.).

After being washed with 10 per cent. solution of pyridine they are passed into the reducing solution, which must be freshly made and is as follows:—

17 c.c. pyridine.
10 c.c. acetone.
99 c.c. of a 4 per cent. solution of pyrogallic acid in distilled water.

The reduction should be allowed to continue for several hours, after which the fragments are dehydrated, treated by xylol, and cut in paraffin; the sections should not be thinner than 5 μ. Staining is done by the same method as the original one of Levaditi. Some other writers prefer that of staining the sections with iodine green; while others again advise freeing the preparations from reduced silver before using the ordinary methods of staining.

As many observers have taken objection to those methods by which spirilla are shown, not by staining only, but by reduced silver, some have endeavoured to discover a method of staining spirilla in sections other than those of Bertarelli and Volpino and that of Levaditi and Manouélian.

Schmorl,[100] whose talent in technique is appreciated by all the world, would appear to have recently solved this problem. He fixes his sections in a solution of 4 per cent. formol; from this they are removed by a sterilized glass rod and put into a solution of sterilized water contained in a perfectly clean glass dish. They are then put into Giemsa's staining solution, contained in a drop of water on a slide; there they are allowed to remain for an hour. They are then put into a second staining mixture, and there allowed to remain for at least five hours. They are then washed rapidly in either distilled water or in a concentrated solution of potash alum; in which latter case they must be again washed in distilled water. They are now ready to be stuck to slides, and mounted in either cedar oil or Canada balsam.

The author has succeeded by this method in staining the spirilla of syphilis in two cases of congenital syphilis.

Just as this method of Schmorl has allowed us to stain Schaudinn's organism by those aniline dyes which we use for staining film preparations, it has been lately shown to be possible to demonstrate the presence of spirilla on films by the silver nitrate reduction method. Although this has never yet succeeded in films when used according to the methods we have just described, Stern[101] has described a method which can be well used with films of all sorts of syphilitic products. In this method the films containing the syphilitic material are kept for several hours at a temperature of 37° C. (98° F.), after which they are plunged for some hours into a 10 per cent. solution of nitrate of silver; when the preparation is slightly brown in colour it is taken out of the bath and washed in distilled water.

Thanks to the various methods we have just described for the reader, science now possesses very complete methods for studying the *Spirochaete pallida* in the various conditions in which it occurs in the body.

CHAPTER XI

CRITICISMS AS TO THE PART TAKEN BY THE SPIRILLUM OF SCHAUDINN IN THE CAUSATION OF SYPHILIS

The last methods, of which we have just given an account in the preceding chapter—those of Schmorl and Stern—have a special importance when considering the objections which have been made to the part played by Schaudinn's organism in the aetiology of syphilis.

One would have thought that so many precise facts all in agreement as to the presence of this spirillum in syphilis, and its differentiation from other spirillar forms, would have sufficed to satisfy us that it is really the specific cause of syphilis, despite the impossibility, up to the present, of obtaining pure cultures of the organism, by which means syphilis could be reproduced. Nearly forty years have passed since the discovery of the spirillum of recurrent fever, during all which time, although no cultures were obtained, it was without hesitation considered to be the cause of the disease; and yet no contradiction of the accumulated facts was made. Nay, further, it is the same in the case of trypanosomes, whose importance as the cause of so many infectious diseases is admitted by everybody.

Yet, despite all this, ever since the publication of Schaudinn's discovery there has been no cessation to the objections which have been made as to its value in connexion with the etiology of syphilis. These objections more especially came from authors who had already pleaded the importance of *Cytoryctes luis* as a cause. First among these was *Thesing*,[102] who declared that Schaudinn's spirillum did not really come from syphilitic products at all, but was simply introduced in the various solutions made use of in the work. After having found some organisms in

Giemsa's solution, Thesing declared that the *Spirochaete pallida* came from this mixture in the same way. It was, however, very easy to refute this objection, as Schaudinn had actually made the discovery when using fresh material, in which medium the spirilla were living and moving under the eye of the observer.

However, this refutation did not discourage his adversaries : far from it ; they proceeded to frame a regular indictment gainst the *Spirochaete pallida* as the cause of syphilis, and although at the present time only a very few observers of any note remain on their side, it is, all the same, proper that we should take some notice of the principal objections.

This task becomes more easy, thanks to the appearance of two recent papers by *Saling*,[103] in which he has collected together all that can possibly be said on the subject. According to this author, the *Spirochaete pallida* is a saprophyte which develops with great ease in the cutaneous lesions of syphilis, and is only found in internal organs in hereditary syphilis of the foetus and the new-born child, where it is generalized in the same way as the common bacillus of the digestive tract.

The principal argument by which Saling tries to prove his contention is the following :—The spirillum of Schaudinn has never been obtained in the internal organs of syphilitic monkeys, which organs are nevertheless very virulent. Saling applies himself to many experiments to prove this fact, which he considers to be absolutely established. Here is an extract from his work :— 'Although every year hundreds of syphilitic monkeys are examined, no spirilla are to be found in the " extremely virulent organs ", except in one case of Zabolotny [which we have already quoted in the third chapter (chapter VII)]. This case is merely an exception to the rule.'

I myself can testify, from a good deal of knowledge in the matter, that of the large number of syphilitic monkeys which are under observation in different laboratories by far the greater number have never been examined from the point of view as to whether their internal organs contained spirilla at all. Indeed it would have been a useless waste of time to constantly make this examination, for these organs are very far from being 'extremely virulent', as Saling so often affirms. Indeed, it has already been shown by Neisser and his fellow workers that there are only some special internal organs of monkeys which contain the virus at all. These are, more especially, the spleen, the marrow of the bones, the lymphatic glands, and the testicle. Moreover, in order to produce a primary lesion, it is necessary to inoculate a very considerable quantity of the pulp of these organs, and in order to get a positive result, material must be taken from many cut surfaces of an organ, or else the pulp of an organ must be inoculated after the whole organ has been thoroughly shaken up, yet even in these cases inoculation does not always produce a primary lesion.[104] Now as the syphilitic virus is so active that the very smallest quantity will produce infection, we can well believe that spirochaetes must be very rare indeed in the internal organs of infected monkeys. In order to justify his research it should be the case that the virus of these organs is exceptionally strong, and this is far from being the case, despite Saling's assertions.

The specific spirillum has been searched for in tertiary lesions in man far more than in the organs of syphilitic monkeys. For a long time the attempts to prove its existence in tertiary lesions failed, and this led us to believe that the organism is to be found here in some other stage of existence. But, as we have before mentioned, in the end it has been found in its spiral form, only the organisms are very few in number and very unequally distributed in tertiary syphilis.

These facts will be seen to be in perfect accordance with the knowledge that tertiary products are only virulent in exceptional cases, and that in order to produce a lesion by inoculation the material used must be taken not only from the softened parts but from the very same peripheral layers in which the syphilitic spirilla have been found to exist. If these were nothing else but simple saprophytes, why is it that they do not increase in gummata, and are only to be found in syphilitic lesions of all kinds, and never in other cutaneous affections? The *Spirochaete refringens*, on the other hand, which *is* a saprophyte, is found in lesions other than syphilis, and in the different products of the genital organs. There is, therefore, no justification to the theory of the saprophytism of *Spirochaete pallida.*

A great number of observers have endeavoured to deny the microbic nature of the spiral filaments which are stained by aniline dyes. Thus *Omeltchenko*[105] affirmed that they are nothing else but fragments of connective tissue which have taken a spiral form. There is no difficulty in disproving this objection; every observer who has any skill in work knows well the pseudo-spirilla which are sometimes found in preparations. But it is only necessary to exercise a very little practice and attention in order not to confound them with micro-organisms in general and with the spirilla of syphilis in particular.

Many have been the discussions on the subject of the interpretation of spirilla in sections stained by means of nitrate of silver. *Walter Schulze*[106] called them by the name of *Silver spirochaetes* (Silberspirochaete), and denied that they have any importance in the study of syphilis. He regards them as being the débris of nervous filaments and of elastic connective fibrils which resemble spirilla but have no true connexion with them at all. Saling[107] and some other workers agreed with this opinion, which they held with great tenacity.

Now it cannot be denied that certain filaments of the tissues can be stained black by silver nitrate, and may then somewhat resemble spirilla. But it is not difficult to distinguish them, and those observers who have some experience in the study of spirilla have been able to do this without hesitation.

Schulze's first paper immediately provoked Levaditi's reply,[108] in which he brings a number of arguments to bear which ought to suffice to refute all objections. The black spirilla in sections of syphilitic lesions are found exactly in the zone which is affected by the syphilitic lesion, whilst the secondary organisms and, amongst others, the *Spirochaete refringens*, are to be found in the superficial layers. The *Spirochaete pallida* of syphilis is to be found not only in the tissue, but also in the lumen of the blood and lymphatic vessels, where it closely corresponds with the spirilla of septicaemia in fowls, and of recurrent fever, both of which are stained black in just the same way by nitrate of silver.

It is still harder to understand the zeal with which the microbic nature of '*Silver spirochaetes*' has been denied, as the very same tissue, when examined in a living state or stained in film preparations by Giemsa's method, shows a large number of spirochaetes absolutely characteristic in appearance.

In his later work Saling insists most of all on the importance of *Karlinsky*'s preparations, which show '*Silver spirochaetes*' in the macerated foetus of a pig. To judge from his photographs[109] these filaments closely resembled true spirochaetes, but Saling is quite wrong in thinking that there is anything in this fact which can impeach the value of Schaudinn's spirillum.

The sow in question was killed in the end, and the autopsy and microscopical examination showed no lesion at all, but the entire litter of six were dead and macerated. In sections from one of these treated by Levaditi's method, spiral filaments were found in great abundance. Hoffmann, to whom these preparations were submitted, did not hesitate to declare that these closely resembled true spirochaetes. Instead of drawing the conclusion from these facts that the pig should be joined to other mammalia, such as man, the ape, the horse, the ox, the sheep, mice, &c., all of which are subject to spirillar diseases, Saling endeavours to use it to refute the microbic nature of the spirillum of syphilis. He rests his opinion on the fact that the mother sow had no lesion at all, and that her body did not contain spirilla. But, while we admit the accuracy of this fact, there is ground for thinking that the mother was able to overcome the same spirilla which brought about the death of the offspring. It is true that Saling affirms that a farm hand had beaten the sow, and that 'the death of the foetus could only have been brought about by the injury' (p. 343), but it must be evident that this theory cannot possibly be considered as a well established fact.

It is quite useless to enter here more fully into the details of the question of the '*Silver spirochaetes*', as a great number of scientific men of very great note, amongst whom I may quote Benda,[110] Blaschks,[111] Gierke,[112] Hoffmann,[113] Levaditi (loc. cit.), Orth,[114] and others, have to a great extent refuted all the arguments of Schulze and Saling.

Amongst other objections taken to the aetiological part played by Schaudinn's spirilla, great capital has been made of the strong resemblance of this organism to other spirochaetes. Thus, *Kiolemenoglou and Cube*[115] affirmed that the spirilla observed by them in fragments of tissues which had nothing to do with syphilis—such, for example, as in ulcerated cancers—could not be distinguished from *Spirochaete pallida.* Schaudinn and Hoffmann, who were able to observe the preparations of these authors, declared, on the other hand, that there was an absolutely distinct difference between the two varieties of organisms.

It is, however, certain that among the large number of spirochaetes now known there are some which resemble very closely that of syphilis. Among these are some of the spirilla of the mouth.

But it is more especially the organism described by Castellani[116] in Yaws, or the framboesia of tropical regions, which presents a very striking analogy to Schaudinn's spirillum. Castellani has called it by the name of *Spirochaete pallidula*, and considers it as the aetiological cause of this disease. This discovery has been confirmed by several observers, amongst whom is Prowazck,[117] who recognized, nevertheless, some morphological differences between the two species. According to him, in the spirillum of Yaws the curves are less steep and more irregular than those of the organism of syphilis; the former spirillum has flattened curves which distinguish it from the latter. I myself have had the opportunity of observing the spirilla of Yaws in Levaditi's films; and I also was able to distinguish the differences between it and that of syphilis.

But in spite of all this, the relationship between the two species is very great. Nevertheless, very far from serving as an argument against the aetiological rôle which is attributed to them, the resemblance would seem to me only to confirm it the more. Here, indeed, we have two different chronic affections whose very close analogy must be clear to every eye, and in both of them we constantly find in the depth of the lesions two different forms of a spirillum which present an astonishing resemblance to each other. Surely then it is clear that we have here to do with two infective agencies whose relationship is similar to that which we know so well exists between the bacilli of tuberculosis and leprosy.

It should be quite enough to look round at the whole of the bacteriological facts which have been collected on the subject of syphilis, in order to be able to assure oneself that, in spite of the impossibility of cultivating Schaudinn's microbe and of obtaining experimental syphilis by means other than that of inoculation with syphilitic products, it is indeed the *Spirochaete pallida* which is the microbe of syphilis. We should recognize that the description of *Cytoryctes luis* was very useful in stimulating the research which brought about the discovery of the cause of syphilis, and acknowledge the value of the large number of objections raised against the aetiological part of the spirillum. For the refuting of these objections has, in turn, very much increased the importance of this organism.

CHAPTER XII

PRACTICAL APPLICATION OF THE RECOGNITION OF THE ORGANISM OF SYPHILIS

Although the microbiology of syphilis cannot possibly be considered as a closed chapter, it is nevertheless certain that it has now gained possession of certain facts of very great importance, not only from a theoretical point of view, but also because of their practical application. It is perhaps the diagnosis of syphilis which profits most of all from the progress which has been made in its bacteriology.

It is by no means rare to meet cases of venereal disease where it is difficult to be sure of the nature of the infection. Sometimes we have to deal with mixed infection, and at other times with lesions whose characteristics are often very indefinite or are wholly absent. Much valuable time is often lost in doubtful cases by waiting for the secondary manifestations of syphilis, and for this reason anything that can make the diagnosis more clear in these cases should be most favourably accepted.

Soon after Schaudinn's discovery, Hoffmann[118] submitted to bacteriological examination many primary lesions taken as soon as possible after their first appearance. He has more especially studied some whose clinical diagnosis could not have been made very definitely; and he found in six of these cases that where the microscope revealed the presence of *Spirochaete pallida* the subsequent course of the disease justified the diagnosis of syphilis.

After these facts had been confirmed in a very large number of cases, Hoffmann[119] formulated the following opinion: 'The diagnostic value of *Spirochaete pallida* in primary lesions, and, above all, in recent chancres, is of great practical importance, for a clinical diagnosis is very often imperative in these cases.

The presence of these organisms justifies a decisive conclusion, although the negative result of the bacteriological examination has no great importance. In those cases where we have to do with the differentiation of exuding papules, with more or less ulcerated surfaces, or with herpetic erosions which resemble them very closely clinically, the presence of *Spirochaete pallida* is of very definite value. In those cases which are not suspected to be the cause of the glandular enlargement, the result of their puncture according to my method should settle the question.'

In a very detailed and careful work, Roscher[120] gives us many facts which confirm the diagnostic importance of *Spirochaete pallida.* Heller and Lydia Rabinowitsch[121] are rather less encouraging, for they think the search after this organism, from the point of view of practical diagnosis, is not to be recommended. But we must observe that their results were obtained with quite an insufficient number of preparations, and they used exclusively films stained by Giemsa's mixture. Much more positive are the facts given by Danziger,[122] who was able by bacteriological examination to make a diagnosis in five cases of syphilis, where clinical examination was useless: usually he examined insignificant erosions of a very indeterminate nature, sometimes even without a trace of induration. Where the presence of *Spirochaete pallida* showed the syphilitic nature of the lesions, the ultimate course of the disease in every case confirmed the diagnosis.

Besides the case of lesions at the very outset, in which bacteriological examination can be of the very greatest use, the certainty of the presence of Schaudinn's spirilla may again be very useful in those cases where syphilitic lesions are well developed, and which may even be in process of cure, although they do not present sufficient clinical characteristics for diagnosis. It is exceedingly interesting in this connexion to note the cases studied by Danziger; he had to do with a case which entered the hospital for the cure of leucorrhoea. On examining the patient, a flat ulceration, very little indurated, was found on one labium minus; the patient was ignorant of its presence. Some short time afterwards typical spirochaetes were found in this ulceration, which was by that time completely healed. Later on the patient had a papular eruption of the trunk and extremities, which confirmed the diagnosis.

It is thus clearly shown that in all cases, easy though they may be to distinguish by ordinary clinical examination, a microbiological diagnosis is indispensable. Thanks to the use of the ultra-microscope, this work is now rendered rapid and easy. Indeed every clinic should introduce this apparatus, which should be used by some one who has experience in searching for spirilla and distinguishing their different species. Very often a glance through the microscope or an examination of a very few minutes' duration will suffice to give a most definite opinion.

With regard to prognosis, although according to some observers the disappearance of spirilla should indicate a cure, a great number of facts in our possession contradict this assertion ; for we may often find that the cure is of a most temporary character, and almost at the very moment that they disappear the spirilla may reappear afresh.

Hoffmann (loc. cit.) insists on the utility of bacteriological diagnosis in the treatment and prophylaxis of syphilis ; for once the lesion has been diagnosed at its very beginning, during that phase which, so far as clinical diagnosis shows, is indefinite, we can at once proceed to excise the lesion, and this may, perhaps, facilitate the cure. This accurate diagnosis must of course be of enormous value in prophylaxis, by eliminating from the beginning an important source of infection.

Thus we see, by all the facts which have been quoted in this article, that in the light of recent events, up to the present time, the microbiology of syphilis *has already rendered enormous service to humanity.*

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PLATE V

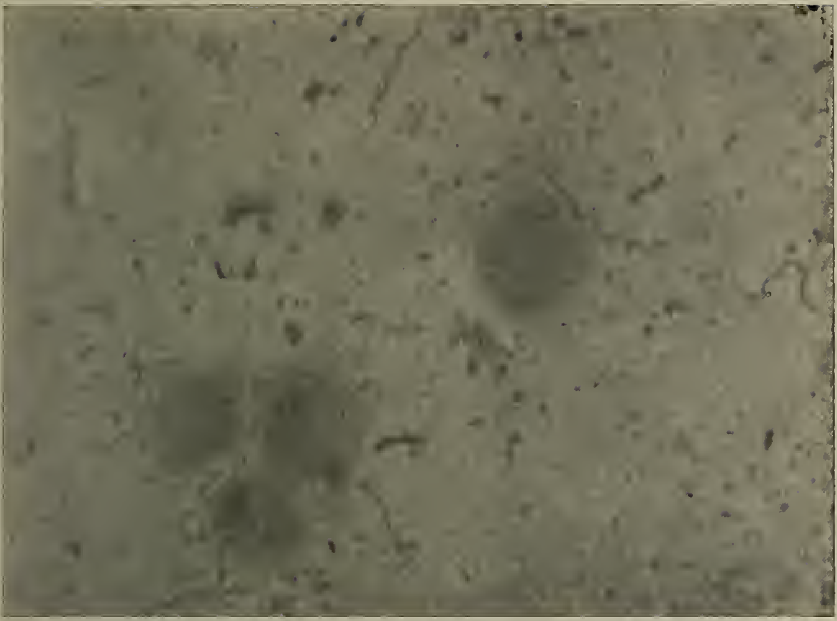
a. Donne's '*Vibrio lineola.*' 1834.

b. Stassano's parasite of syphilis. 1901.

c. *Cytoryctes luis,* after Siegel. 1902.

d. Spirochaete pallida from a primary lesion in a chimpanzee.
a Spirillum undergoing division; *g* red corpuscles. (Giemsa's method.)

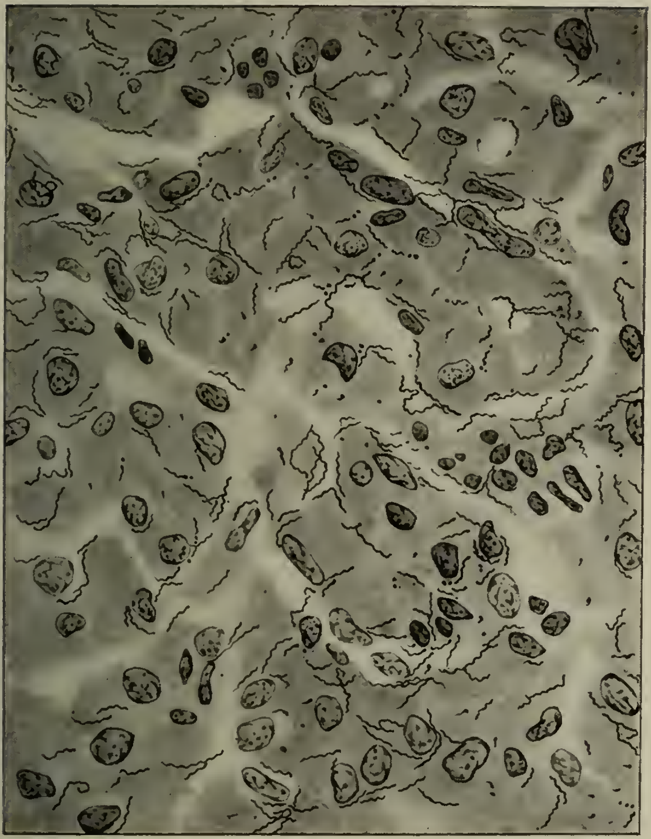
PLATE VI



Spirochaete refringens. Photomicrograph of a film preparation. Magn. 7000 diameters.

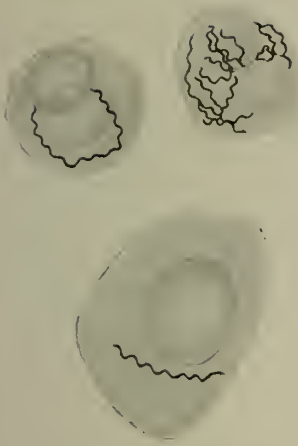
Spirochaete pallida. Photomicrograph from the fluid of a vesicle. Magn. 7000 diameters.
From photomicrographs by Staff-Surgeon Richards, R.N.

PLATE VII

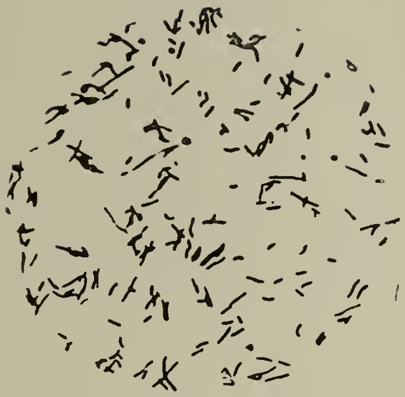


Spirochaete pallida in the liver of a new-born child.
(Stained by Levaditi's method.)

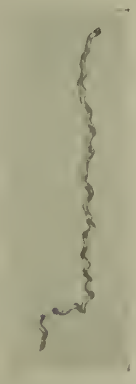
Plate VIII



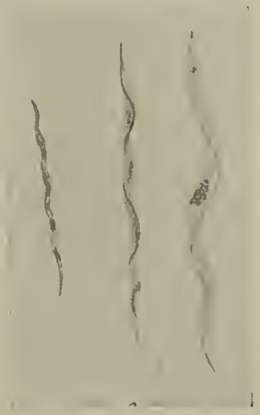
a. One mononuclear and two polynuclear leucocytes, all containing the spirillum. After one of Dr. Gierke's preparations, stained by Levaditi's method. 1907.



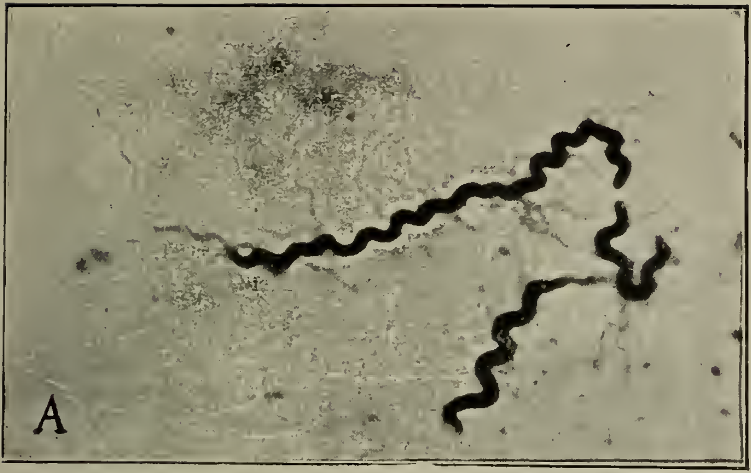
b. Cholera vibrios in culture.



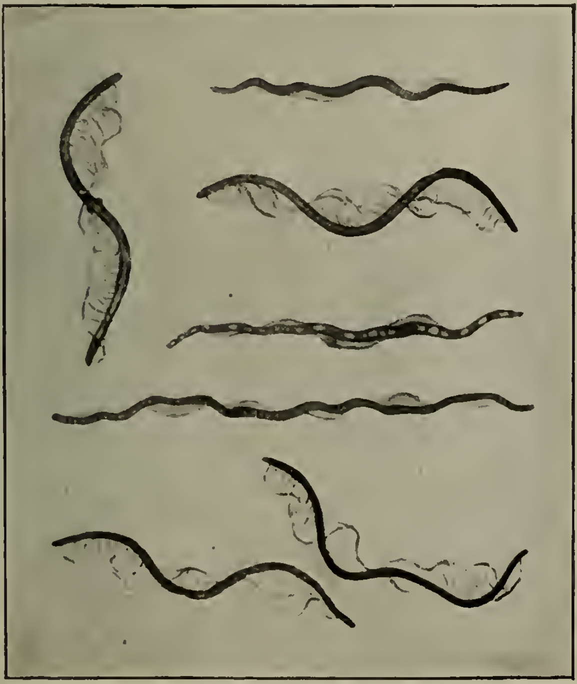
c. Vibrio of cholera in the form of a flexible spirochaete.



d. Trypanosomes passing into the shape of a spirochaete. (After Schaudinn, 1905.)

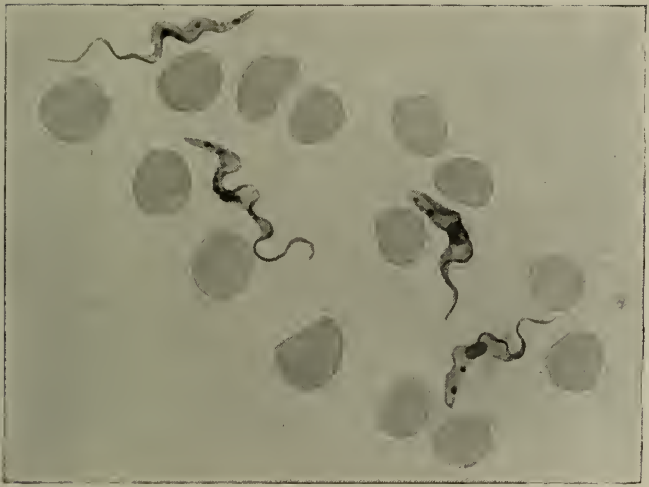


a. Spirochaete Gallinarum, with *Vibratile Cilia.* (After Borrel.)

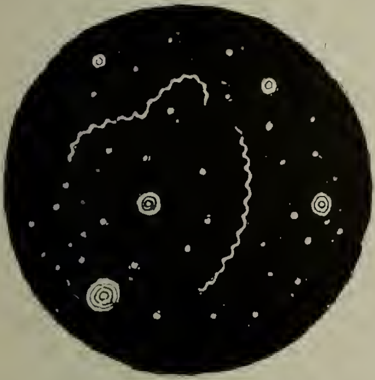


b. Spirochaete Balbiani. (After Borrel.)

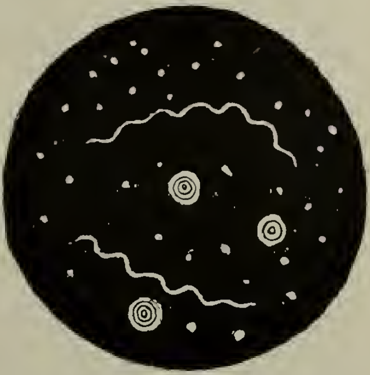
PLATE X



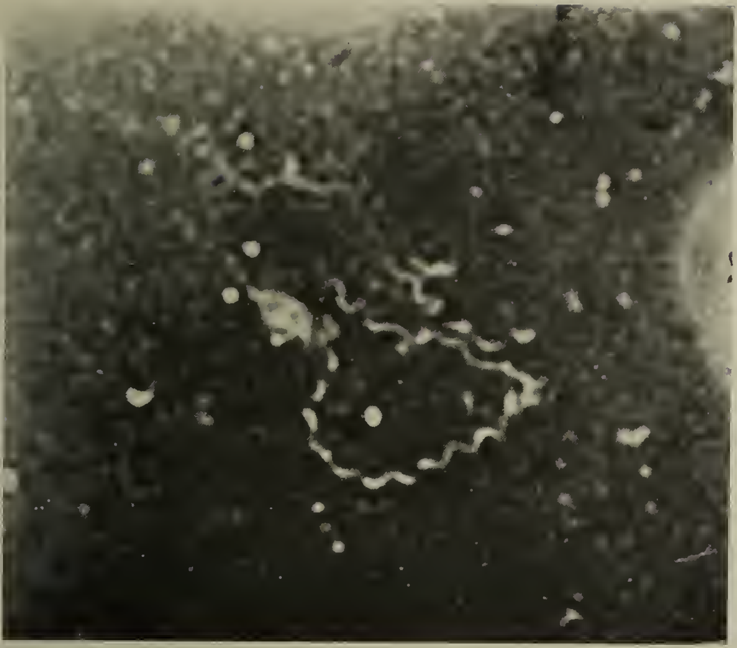
a. Trypanosoma Gambiense; from rat's blood film preparation. Note undulant membrane.



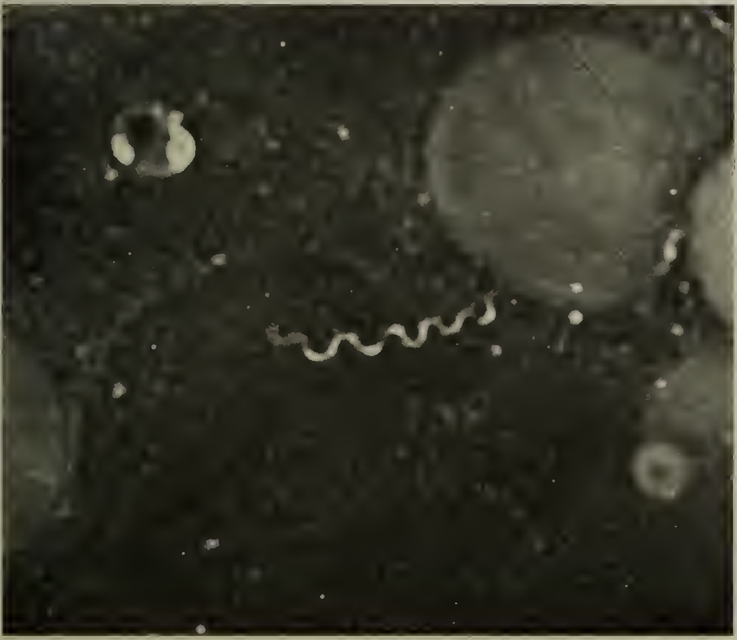
b. Spirochaete pallida, on dark field in Reichert's ultra-microscope.



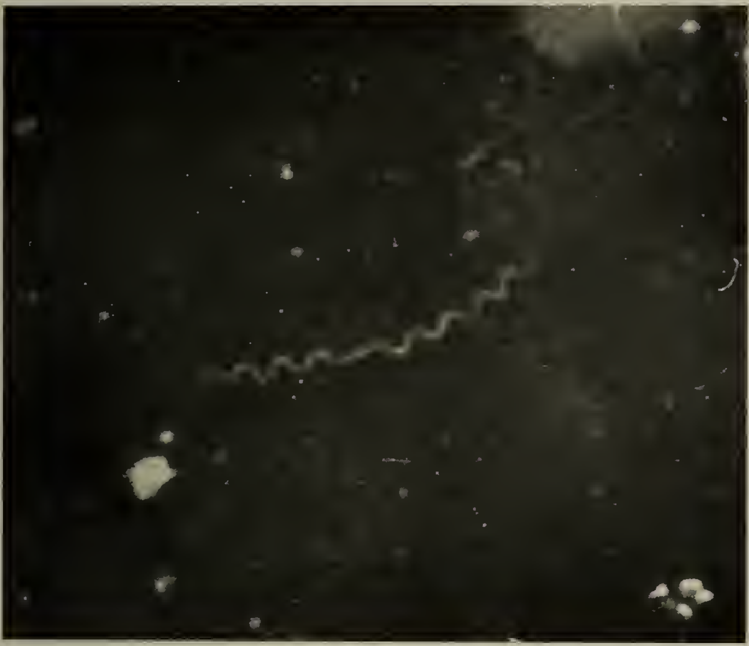
c. Spirochaete refringens, on dark field in Reichert's ultra-microscope.



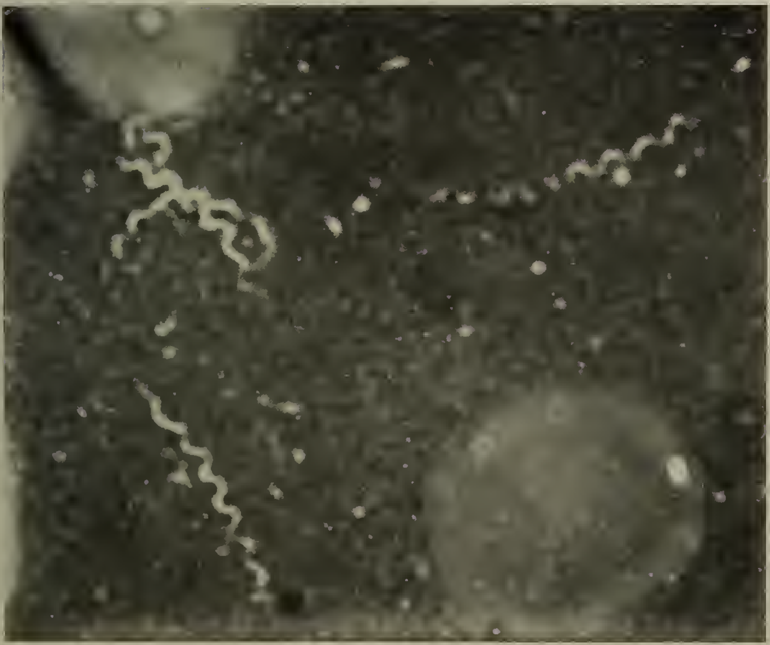
a. Spirochaete pallida. Photomicrograph under high magnification. Photographed by reflected light.



b. A specimen of *Spirochaete pallida.* Photomicrograph. Magn. 4500 diameters. Photographed by reflected light. The circular body above the *Spirochaete* is a red blood corpuscle.



a. Spirochaete pallida.



b. Spirochaete pallida.

Plate XIII.

Spirochaete pallida from a condyloma where the organism was unusually plentiful. Film preparation stained by Leishman's method. × 1000.

(*From a film kindly lent by Lieut.-Col. W. B. Leishman, R.A.M.C.*)

(*A. M. Kelley, del.*)

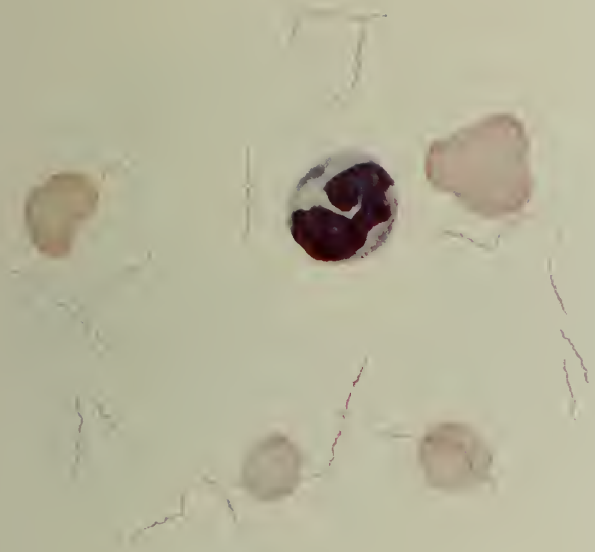


PLATE XIV.

Spirochaete pallida in the spleen of a macerated foetus, stained by Levaditi's original method. × 1000.

(*From a specimen kindly lent by Lieut.-Col. W. B. Leishman, R.A.M.C.*)

(*A. M. Kelley, del.*)

PLATE XV.

Spirochaete pallida from the lung of the same case shown in the preceding plate. Stained by Levaditi's original method. × 1000.

(*From a specimen kindly lent by Lieut.-Col. W. B. Leishman, R.A.M.C.*)

(*A. M. Kelley, del.*)

PLATE XVI.

Spirochaete pallida from the macerated spleen of a syphilitic infant, stained by Levaditi's method and counterstained with polychrome methylene blue. × 1000.

(*From a specimen of Lieut.-Col. W. B. Leishman, R.A.M.C.*)

(*A. M. Kelley, del.*)

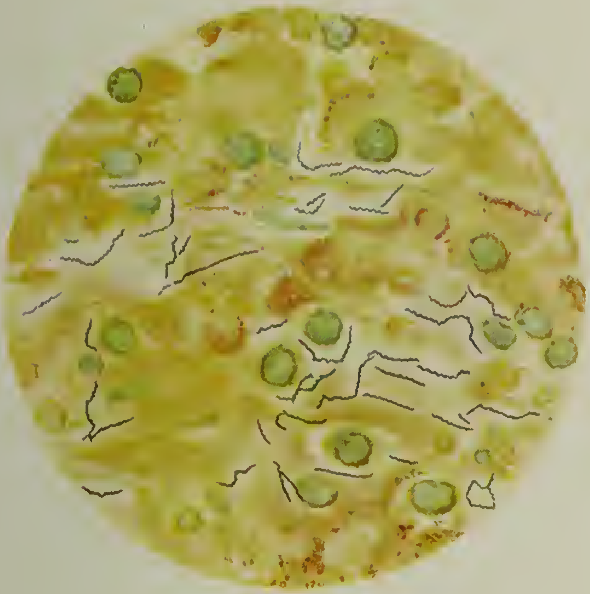


PLATE XVII.

Drawing of *Macacus cynomolgus*, showing typical primary lesions over eyebrows, six weeks after inoculation with syphilitic products.

THE GENERAL PATHOLOGY OF SYPHILIS

BY

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CHAPTER XIII

THE GENERAL PATHOLOGY OF SYPHILIS

Syphilis is in many respects unique amongst the infective diseases of mankind. It combines the characters of a specific fever running a very chronic course with those of an infective granuloma. No other communicable disease is apt to continue its manifestations twenty or even fifty years after the original infection, and, when it would appear at an end, syphilis may leave its victims subject to chronic degenerative changes, especially of the central nervous system, not in themselves of a directly syphilitic nature. Further, it is a disease which is more clearly inheritable than any other known infection.

The Specific Nature of Syphilis. Nothing is more certain than the fact that syphilis is a strictly specific infection. The idea that it is a filth-disease, originating from unclean and promiscuous sexual congress, is entirely disproved by the data of exact pathology. How in the first place it arose is a matter of pure conjecture. We must presume that the infecting agent was in the beginning a harmless genital saprophyte, and that it has since acquired parasitic powers enabling it to invade the living tissues and induce widespread morbid reactions. Having in some way thus originated, we see the disease to-day spreading from case to case by direct infection, able to attack the chaste as well as the unchaste, should transfer of the virus take place from an infected to a normal person, irrespective of sexual intercourse.

The history of medicine abounds in examples of diseases long confounded with allied affections, but in the end, with the advance of clinical observation and experiment, gradually recognized as specific entities. All venereal diseases were at one time confused together. Gonorrhoea was at length recognized as an independent affection ; later still, venereal sores were found to fall into two groups—those which after weeks or months are followed by symptoms of constitutional infection, and those which produce no such results. There are few nowadays who doubt that the 'soft sore' is a distinct infection, which may indeed complicate true syphilis at the outset, but is in no sense a mere abortive form of that disease.

Syphilis now stands out as an affection well marked and separate from other venereal diseases. It would be rash to predict that no further differentiation amongst these infections will ever become manifest, but there is at present no hint that syphilis is other than a specific entity. Recent discoveries have indeed greatly strengthened this belief.

The Effect of Modern Discoveries as to Syphilis. The absence of exact knowledge as to the nature of the infecting agent in any given infective disease has always proved a serious bar to its scientific study. Even a graver hindrance is the lack of any susceptible animal suitable for experimental investigation of the infection. With Koch's discovery of the tubercle bacillus our knowledge as to tuberculosis at once began to increase by leaps and bounds, and is still advancing. But in the case of syphilis pathology seemed to have reached a limit. What morbid anatomy and histology could teach had been learned; experimental inoculation upon human beings was not justifiable upon the scale required. Chance clinical observations occasionally allowed of some new, though mostly tentative, conclusion to be reached, but the subject was almost at a standstill. Then came the announcement by Metchnikoff and Roux, in 1903, that syphilis was inoculable with typical results on the anthropoid apes, and in less typical fashion upon certain of the lower monkeys—a discovery confirmed on every hand. Again, two years later, came the evidence brought forward by Schaudinn and Hoffmann connecting the *Spirochaete pallida* with the causation of syphilis. This evidence, it is true, is circumstantial only, but it has been so abundantly confirmed that the spirochaete has gained widespread acceptance as the true causal agent in the disease.

It is difficult to say which of these two discoveries is the more important. Up to the present time the possibilities opened out by simian inoculation have probably proved the more fruitful in direct positive advances in our knowledge. The inoculability is a tangible fact which cannot be gainsaid. It has already afforded the means for tracing the generalization of the syphilitic virus throughout the body, and has in many ways corrected the crude data which had been derived from clinical observation ; it makes it possible to distinguish between a cured and a latent case of the disease, while the problems of immunity can for the first time be approached by those modern methods which have proved of such value in the case of other infections. We have, too, a criterion by which the reality of the alleged successful results of syphilitic inoculation upon other animals can be judged. The discovery of the spirochaete may, it is true, in the long run, prove the more important, but at present there are certain limitations to its value, some of which must remain until it has been found possible to cultivate the organism. So far it fulfils only the first of Koch's postulates, but it does this very fully. The technique of its demonstration is often difficult and uncertain, though less so with experience; nevertheless, the inoculation of apes appears at present a more certain test as to the syphilitic nature of any given material than the presence or absence of demonstrable parasites.

The evidence connecting the *Spirochaete pallida* with syphilis is fully discussed in another section of this work [Vol. I, p. 95–101.] While I accept it as in all probability the causal agent, I shall endeavour, in this article on the general pathology of syphilis, to confine myself as far as possible to such facts as would remain true even should it be proved that the spirochaete was not the cause of the disease. Though I shall frequently have to refer to the spirochaete, I shall, wherever possible, use the term 'syphilitic virus'.

The Properties of the Syphilitic Virus. Syphilis has always been recognized as a 'contagious' disease in the strict sense, i.e. one which spreads by direct infection only. The reason for this is clear : it depends upon the very low resistance of the virus outside the human body. Tested by inoculation upon apes, it remains efficacious only up to six hours after its removal from the body. It is destroyed by heating for an hour to 51° C. Hence it is that syphilis is so rarely conveyed indirectly. Where a cup or tobacco pipe is used in common by a syphilitic and a healthy subject, so that still moist secretions may be transferred, infection may undoubtedly arise in rare cases. But in the overwhelming majority of cases the disease is transferred by immediate contact, usually in sexual intercourse (90 to 93 per cent. of all cases, according to Fournier), more rarely in kissing or suckling, or in the surgical examination of a case of active syphilis. The conveyance of syphilis by inheritance will be discussed later.

The Channel of Infection. Clinical experience proves the primary seat of inoculation in acquired syphilis to be almost invariably a surface covered by squamous epithelium. This is so in all cases of syphilis of the genital organs in both sexes, for in the male the urethra, beyond which primary inoculation does not occur, and in the female the cervix uteri, of which the same is true, are both covered by epithelium of this type. The mouth, tongue, tonsils, and pharynx are similarly coated. Practically the only instance to the contrary which can be cited is primary chancre of the rectum above the sphincter ani—an occurrence of such extreme rarity that it only emphasizes the general law laid down. It would seem as if squamous epithelium were the specific primary nidus of infection. In order to effect a lodgement, the parasite would appear, in the great majority of cases, if not always, to require some minute crack or abrasion in the epithelium. Whether infection ever occurs through intact epithelium or mucous membrane cannot certainly be decided, but it is at least clear that minute surface-lesions, such as are apt to occur during coitus, are conditions very strongly predisposing to infection.

Experiment has carried our knowledge to a still further point of certainty. Cutaneous inoculations are alone successful. There seems only one way of producing syphilis in apes and monkeys, namely, introduction of the virus into the scarified epidermis. It is strange but true that an organism capable, in the later stages of the disease, of flourishing in so many of the bodily tissues, should at its first introduction be capable of taking root in one tissue only—the epidermis, and that a damaged epidermis. In all the numerous experiments of Neisser and his colleagues, the rubbing of virulent material into the undamaged surface of the tonsil, conjunctiva, and nasal mucous membrane produced no effect. They were uniformly unsuccessful in fifty-one cases in which subcutaneous inoculation was tried, though many animals so treated became cachectic and died. Equally futile was intravenous inoculation, which they attempted fifteen times. Intraperitoneal inoculation has also proved of no avail. These non-cutaneous methods may indeed lead to the formation of antibodies in the inoculated animal, but they do not cause recognizable syphilis. The only possible exception to the rule seems to be the testis: of two animals inoculated in the incised testis, one subsequently proved refractory to cutaneous inoculation, and the other, killed after fifty-six days, was proved to harbour the virus in its bone-marrow. Primary infection of the testis cannot occur under natural conditions, and the results of experiment upon apes tend to confirm clinical experience, that the acquired form of syphilis is propagated exclusively by cutaneous channels.

As regards experimental inoculations upon the relatively insusceptible lower monkeys, it would seem that success can be achieved only in certain regions of the body, namely, the genitalia and eyebrow. It has been suggested that this depends upon the greater vascularity of the skin in these parts ; Neisser states that he has never attained a successful result without such energetic scarification as to cause some haemorrhage.

The rule that cutaneous inoculation is alone successful does not apply to the inherited disease.

The General Course of Syphilis. Before pursuing in detail the progress of the infection throughout the body, or discussing the essential nature of the lesions which arise, it will be convenient to make a few general observations on the course of the disease.

Attention has frequently been called to the correspondence between syphilis and the specific fevers ; the difference is indeed mainly one of chronicity. An ordinary specific fever, such as small-pox or scarlatina, presents certain definite stages. After exposure to infection there is a latent period during which no clinical manifestations are evident : this is the stage of incubation. The specific agent is at work, but until it has so multiplied in the body as to produce a sufficient toxic influence, the body does not respond by any clinically recognizable phenomena. The latent period may be short or long—a day or two in scarlet fever; a fortnight or so in typhoid. Then comes the bodily reaction against infection—in some cases abrupt, in other fevers insidious in onset. The popular idea dates the beginning of the disease from the first clinical manifestations, but in truth the process starts at the time of infection.

In most fevers there ensues a cutaneous eruption or exanthem, varying in character and time of onset with the nature of the disease. The exanthem may effect mucous as well as cutaneous surfaces. And finally, if recovery take place, the bodily reaction ceases, the temperature falls, the eruption vanishes, and health is restored. Nevertheless, in many cases the disease leaves some traces behind—a weakness, an anaemia, or a slowly progressive change in one or other organ which has been affected.

In all these respects syphilis corresponds with the ordinary specific fevers. There is an incubation period, followed by a rise of temperature and an exanthem, with general disturbance of the health. And when all this has subsided there remains a tendency to remote consequences of a very special character. But there is this difference between syphilis and the ordinary fevers: instead of running its course in a few weeks, its manifestations are spread over months and years. The incubation period is longer than in other fevers, the febrile reaction and rash may persist for months, and the ultimate sequelae may appear after ten or twenty years. Syphilis may justly be classed, from this aspect, as a chronic specific fever.

From another aspect it may with equal propriety be classed with the infective granulomata. An acute infection such as that seen in tissue-invasion by the pyogenic cocci, running its course in a few days or weeks, is met by a response on the part of the more labile factors in bodily defence—notably of the polynuclear leucocytes; there is no time for the more sluggish reaction of the cells concerned in tissue repair, though this is added during the later stages of healing. But in such chronic tissue-infections as that due to the slowly-growing tubercle bacillus the primary reaction is on the part of the endothelial and connective-tissue elements of the body; the leucocytes take but a subordinate share in the process. The first result of the lodgement of tubercle bacilli in the tissues is, as a rule, the formation of a kind of granulation tissue, constituting the primitive tubercle. Such infections are hence termed 'infective granulomata', and they tend, on the one hand, to a degeneration and softening of the newly-formed tissue, and on the other to a fibrosis which helps to limit the spread of the infection.

The nature of the tissue reactions in syphilis conforms to this latter type. The primary seat of inoculation becomes occupied by a granulomatous growth—the chancre—which consists essentially of cells derived from the fixed connective-tissue and endothelial elements with an abundance of 'plasma cells', the origin of which is not yet certain, but which are clearly not among the more labile elements in tissue defence. Most of the cutaneous lesions of the eruptive stage of syphilis show similar aggregations of plasma-cells, which, though they may not organize into permanent fibrous tissue, indicate an analogous reaction. But it is in the later stages of the disease that the correspondence with the infective granulomata is most clearly apparent. When the eruptive fever is over, there remains, so long as the virus persists in the body (which may be almost for a lifetime), a tendency to local tissue-proliferations, or gummata, which present the closest analogy with tubercle. So similar is gummatous to tuberculous infiltration, that, though it is easy to indicate general differences, the histologist is not rarely in some doubt as to which process he may be observing. Syphilis in this stage appears as an infective granuloma pure and simple.

Last of all, the final and most remote effects of syphilis—the so-called 'parasyphilitic' lesions—are in their essence degenerative changes associated with overgrowth of the fixed connective tissue elements.

The Detailed Course of Syphilitic Infection.

Incubation Period. The essentially chronic nature of syphilis is seen even from the first. After the virus has been introduced into the skin, there ensues an incubation period of several weeks, during which not even a local manifestation is apparent. In man this latent period may last from ten days to seven weeks, but on an average it is three weeks or a month. In apes and monkeys it is about the same: according to Neisser's figures the average incubation period is three or four weeks, with extreme limits, in exceptional cases, of twelve days and sixty days respectively. Neisser conjectures that the variations depend upon the number of parasites present in the inoculated material. During the incubation period we must believe that the parasite is gradually making good its foothold in the local tissues. The tardiness of the local reaction which it evokes depends upon the fact that it is a reaction of the fixed tissues. If the virus of gonorrhoea or of soft sore has been simultaneously inoculated, their manifestations are speedily apparent, but in due course are followed by the specific reactions associated with syphilis.

The Primary Lesion. The clinical characters of the chancre are dealt with elsewhere in this work. I propose here only to touch on its more general pathological features.

It is essentially a *cutaneous* lesion at the outset, spreading to the subcutaneous tissue and later to the local lymphatics. In cases where the virus has been deliberately inoculated in man, in which alone the earliest stages of the process are likely to come under observation, the first sign to appear is a slight and very local reddening of the skin, which slowly spreads and becomes a raised papule. As it increases in size, a slight crust of dried exudation may form on the surface, and beneath this the epithelium is apt to be superficially eroded, though, as a rule, no extensive loss of substance occurs.

With the spread of the inflammatory reaction to the dermis, which takes place at a comparatively early period, a marked degree of induration is, in most cases, apparent. In part this induration doubtless depends on lymphatic obstruction, but it is in the main due to proliferation of the fixed connective tissues and endothelium, with a local aggregation of lymphocytes and plasma cells. It varies considerably in its degree, but on the whole amply justifies the term 'hard chancre' commonly applied to the primary sore. Many clinical varieties of the chancre have been described according to the degree of induration; they depend on the extent of the reaction on the part of the subcutaneous tissues. This varies in different regions of the body; it is often less marked on the female than on the male external genitalia, and it is sometimes practically absent in extra-genital chancres.

The final stage of the primary lesion is one of gradual disappearance. The induration becomes less, and healing slowly occurs, as a rule with little or no scarring or permanent tissue change. The total duration of the chancre is from four to six, or more rarely eight, weeks. It is a striking fact that the initial manifestations of so dire an infection should be of such apparently benign nature. Almost painless, apparently local, accompanied by no constitutional disturbance, and tending to disappearance in a few weeks, the chancre offers little hint of what is to follow.

The Lymphatic Phenomena accompanying the Primary Sore. In spite of this apparent benignity, there is already one constant sign that the infection is not a merely local one. This consists in an enlargement of the lymphatic glands in the vicinity of the chancre—the 'indolent bubo' so characteristic of the primary disease. 'Pas de chancre infectant sans bubon' was Ricord's law, and Fournier declares that in 5,000 cases he has found it but thrice absent.

The lymphatic vessels passing from the site of the chancre to the nearest lymph-glands soon become recognizable as indurated cords, interrupted here and there by small nodular swellings—the so-called 'bubonuli'. The process is a chronic lymphangitis with local lymphatic infarctions. Even by the end of the first week after the chancre has appeared, certainly during the second week, enlargement of the lymphatic glands is clinically manifest, and there can be little doubt that glandular *infection* is practically concurrent with the development of the chancre itself. The gland or group of glands to which run the lymphatics draining the site of the initial sore, wherever this may be, become gradually enlarged and firm—a change usually unnoticed by the patient, since it is unaccompanied by pain or tenderness. Nor, even at this stage of the disease, is infection necessarily confined to the first group of glands to which the lymphatics in question pass. In persons dying accidentally during the primary stage of syphilis in the genital region, there has been found, in addition to the ordinary inguinal bubo, a marked enlargement of the iliac and even of the aortic lymphatic glands. It is probable that this is no exceptional thing, though it cannot be determined during life.

The truly syphilitic nature of the glandular affection is beyond doubt. It runs the same sluggish course as the primary sore, spontaneously subsiding after a time. The *Spirochaete pallida* has repeatedly been demonstrated in the indolent bubo, and material from such glands has proved inoculable upon apes and monkeys with typical result.

Clinical evidence is at one with histological observation and with animal experiment in pointing to the lymphatic system as the main channel by which the virus of syphilis passes from the primary lesion into the system. Whether it is the only channel is open to question ; there is as yet no clear proof of primary absorption by the blood-vessels, though it would be difficult to disprove such an hypothesis. But the facts already cited as to the early infection of the local lymphatics offer a complete explanation of the well-known truth that even free excision of the primary chancre, when it first becomes manifest, has no influence whatever in preventing constitutional syphilis. It has been seen that the response to primary infection is a very tardy one, with a latent period of some weeks. The response to lymphatic infection may be assumed to be equally slow, and the constitutional disease itself has a latent period which overlaps, or coincides with, the objective phenomena of the primary stage. Slowly the virus spreads from point to point, and the sluggish response of the fixed tissues follows too late on its trail for measures of interception to be efficacious.

The Phenomena of Constitutional Syphilis. During the earlier stages of the disease which have so far been described, there is no general disturbance of health—no response on the part of the body as a whole to the infection which has taken place. This is the so-called ‘ primary ’ stage of syphilis, during which it is an apparently local affection.

Now ensues a stage when the body as a whole begins to react against an infection which has manifestly become general; this is commonly known as the 'secondary' stage of syphilis. The phenomena of constitutional syphilis are very varied, and will here be considered only from a general point of view. The incubation period of the constitutional symptoms is, on an average, six or seven weeks from the first appearance of the primary sore, or between two and three months from the date of infection. Doubtless general infection has taken place some weeks before any outward signs are apparent.

The phenomena of the general bodily reaction are widely different from those of the initial infection. In place of a localised granulomatous formation we see a succession of rashes spreading over the cutaneous and mucous surfaces—widely diffused, though slight, enlargement of lymphatic glands—a chronic febrile condition with anaemia and general disturbance of health—aches and pains in the bones and a tendency to obscure inflammatory changes in many of the internal organs. It is not too much to say that no part of the body is exempt from the manifestations of secondary syphilis, though in any given case but few organs may be affected. Multitudinous though they be, the symptoms tend to preserve a certain general order in their evolution, and they may extend over a year or two unless controlled by active treatment.

The phenomena of secondary syphilis may be divided into general and local, and the local lesions must be regarded as metastatic—i.e. of the nature of local reactions against scattered accumulations of the parasite. Each papule in a cutaneous eruption must mean a local aggregation of the virus in the skin; an iritis in one eye implies a special incidence of the poison upon that rather than upon the opposite iris. Nevertheless, during this stage of the disease, the reactions tend on the whole to be distinctly symmetrical in their distribution. There would seem no reason why a virus generally diffused throughout the body should be unilateral in its effects, though slight and obscure predisposing causes may even at this stage determine the affection of one eye or one testis rather than the other.

In this respect of symmetry of lesion there is a marked contrast between the earlier and the later stages of constitutional syphilis, for in the latter there is commonly no symmetry at all. There is another general difference between the lesions of these two stages, namely, in their local gravity. As a rule, to which, however, there are exceptions, secondary syphilis has much of the benign character seen in the primary stage of the disease. The consequences of secondary iritis may indeed be serious, but the majority of the local lesions of this stage tend to clear up, leaving no permanent trouble behind. Far otherwise is it with tertiary lesions, in which extensive tissue-destruction is common, and irreparable local consequences may ensue.

Lastly, it must be noted that secondary lesions tend to manifest an infective power little if at all inferior to that of the primary sore. It is a notorious clinical fact that the secretions from affected mucous surfaces (syphilitic sore throat, condylomata, &c.) are infectious to a very high degree: the disease is probably far more often conveyed to others during the secondary than during the shorter primary stage. This is confirmed by the results of inoculation upon apes and monkeys: the inoculation of material from secondary lesions is just as successful as where material from the primary lesion is employed, so long, at least, as the disease is in an advancing condition. During retrogression of the secondary lesions much more variable and uncertain results follow inoculation: the virus now appears to be scanty and localized. In correspondence with the above facts is the readiness with which the spirochaete has been found in secondary lesions of all kinds, often in large numbers. In this respect of infective power the manifestations of early constitutional syphilis offer a strong contrast to what is seen in the later stages of the disease.

The General Constitutional Symptoms of Secondary Syphilis. The general health may be little affected during the eruptive stages of the disease: a man may present a well-marked exanthem and yet feel perfectly well. For some reason which cannot yet be explained, the female sex seems to suffer more than the male. Fever and anaemia are commoner in women than in men, and especially in young women.

Syphilitic Fever. A raised temperature in the course of secondary syphilis is far from constant, yet by no means rare. The fever is usually transitory and not of high degree. Slight prodromal or initial fever may at times be observed before and during the eruptive stage, but the more common type of secondary fever appears to be independent of other symptoms. It occurs especially during the earlier months of the secondary period, and, according to Fournier, may be intermittent, continued, or irregular in type. It is associated with malaise, acceleration of the pulse, and other concomitant phenomena in proportion to its degree.

The Anaemia of Secondary Syphilis. In no respect are the constitutional effects of syphilis more constantly shown than in the anaemia which it induces during the secondary stage. The first and slightest degree of the blood change is seen in a fall in the haemoglobin-percentage, habitually seen even before the appearance of the secondary rashes. The haemoglobin may fall to 75 per cent. of the normal without any noteworthy loss in the number of red corpuscles. A somewhat graver degree of anaemia is associated with the outbreak of the cutaneous eruptions. The number of red corpuscles now falls, though rarely to any marked extent; the average count may lie between 4,000,000 and 5,000,000 erythrocytes per c.mm. The relative fall in haemoglobin is greater than this, so that the colour-index is less than unity: in other words the anaemia is of the chlorotic type, and this is said to be especially pronounced in young women. The ordinary anaemia of secondary syphilis does not, then, differ from the secondary anaemias seen in other conditions. It reaches its greatest intensity with the height of the cutaneous eruptions and tends to disappear with these. In the later stages of the disease blood changes may be almost absent, though severe anaemias may be seen at times in the tertiary stage.

As examples of a far more severe type of anaemia in constitutional syphilis, the cases recorded by F. Müller are commonly quoted. Here the red corpuscles and haemoglobin became extremely reduced—in one case to 720,000 erythrocytes per c.mm, with 18 per cent. haemoglobin—the colour-index being thus greater than unity; poikilocytosis was present, with nucleated red corpuscles—even megaloblasts—the condition resembling pernicious anaemia. Such cases are certainly of extreme rarity in acquired syphilis, but in the congenital form of the disease very severe anaemias are far from uncommon, and may be fatal, though they do not, in their essence, differ from other grave secondary anaemias.

There is one consideration in regard to anaemia in syphilis which must not pass without remark. Mercury, so inevitably administered so soon as the diagnosis is made, is itself a drug tending to produce anaemia. How much, then, of the supposed anaemia of syphilis is due to this cause? The answer is not difficult: the anaemia is truly syphilitic. Not only is it present before the administration of mercury, but, for a time, when the mercurial treatment is first commenced, the blood condition markedly improves. Mercury has indeed been called 'the iron of syphilitic anaemia'. Only when the drug has been given for some time does its deleterious effect upon the blood become manifest—a fact which affords good reason for suspending the treatment from time to time.

Leucocytosis in Secondary Syphilis. All observers are agreed that in the eruptive stage of the disease some increase in the circulating leucocytes is present. The increase is usually of only moderate degree, but leucocyte-counts as high as 20,000 per c.mm. have been recorded. There is, further, a general agreement that this increase is not due to the polymorphonuclear leucocytes; it contrasts in this respect with ordinary septic or inflammatory leucocytosis. It is a rule of wide application that a circulatory leucocytosis tends to correspond in its character with the local leucocytoses seen in the lesions of the disease in question. This is so in syphilis. The polymorphonuclear leucocytes play little or no part in the local lesions of the uncomplicated disease: it may be assumed that the syphilitic virus, like that of tubercle, exercises no chemiotactic influence upon this cell. The most abundant cells in the local lesions of syphilis are the lymphocytes and the plasma cells which are by many believed to be closely associated in their origin with lymphocytes. In correspondence with this, the chief element which appears concerned in the circulatory leucocytosis of active secondary syphilis is the lymphocyte. In this connexion may be noted an interesting fact recorded by Ravaut. During the secondary period he found a marked lymphocytosis of the cerebro-spinal fluid, running *pari passu* with the cutaneous eruption; in the case of extensive papular syphilides he found the cerebro-spinal fluid quite turbid with lymphocytes. This was not seen in the tertiary stage unless the eye or the central nervous system were affected.

It has also been stated by Loos and others that a circulatory eosinophilia may be present in secondary syphilis in proportion to the intensity of the cutaneous eruption. The combination of lymphocytosis and eosinophilia is alleged to be suggestive of this stage of the disease.

In the anaemia of hereditary syphilis lymphocytosis is common, as in the other anaemias of infancy, and myelocytes may be present. The following table, calculated from blood-counts quoted by Drs. Drysdale and Thursfield, may be taken as fairly typical of ordinary congenital syphilis:

Haemoglobin	76	per cent.
Red corpuscles	4,224,000	per c.mm.
Leucocytes—		
Polymorphonuclears	6,952	,,
Lymphocytes	5,440	,,
Large mononuclears	850	,,
Eosinophils	54	,,
Myelocytes	67	,,

There is nothing here which is in any way remarkable or different from what might be seen in any moderate secondary anaemia in infancy. Lymphocytosis is so habitual a feature in infantile anaemias that one cannot lay much stress on it. It is impossible to name any one feature in the blood-count which is distinctive of syphilis.

The Local Phenomena of Early Constitutional Syphilis. These, which constitute the general symptomatology of the secondary stage, are fully described elsewhere in this work: only their general features can be considered here.

Whilst the lymph-stream is the path by which, in the main, the virus enters the system, its ultimate diffusion throughout the body must be by the blood. Nevertheless it would appear that the blood itself is not in any way a favourable soil for the multiplication of the parasite, and experiment proves that the circulating blood but rarely yields positive results on inoculation. The blood of active cases of the disease has indeed produced syphilis when inoculated upon human beings, but the far more extensive experiments which have become possible since the susceptibility of apes has been established prove that the virus is present in the blood in small and inconstant amount. Positive results on inoculation are recorded, but they are few in number. In Neisser's extensive series of experiments blood-serum yielded a uniformly negative result : Hoffmann succeeded three times in producing the disease with human blood, once with blood from a case of six months' duration. In accordance with this is the rarity with which the spirochaete has been demonstrated in circulating blood (some fifteen times only). In blood taken from the spleen, or from syphilitic rashes, success has more often been achieved, but in such cases there is, necessarily, admixture with local tissue elements and juices.

It is thus clear that, although the blood may be the channel by which the virus is diffused throughout the body, syphilis is in no sense a septicaemic disease even in its constitutional phase. The type of infection is essentially 'metastatic'. The virus has affinities with certain tissues, and in these, conveyed thither by the blood, it can settle and multiply. Thus arise its characteristic local manifestations, and the known distribution of these affords an index of relative proclivity to the virus on the part of the various tissues.

It has already been seen that primary infection with the disease can occur only by cutaneous channels ; squamous epithelium appears almost the necessary initial nidus, indicating some special proclivity on its part to the parasite. It might be urged that the primary disease must of necessity be so conveyed because the body is everywhere covered with squamous epithelium. But apart from the already mentioned failures to convey the disease artificially by other than cutaneous inoculations, the phenomena of secondary syphilis afford convincing evidence of this special affinity of the virus for squamous epithelium. Although, when diffused throughout the system, the parasite has every tissue in the body at its mercy, there is none which is so uniformly and characteristically attacked as the integument. So constant and conspicuous are the rashes of secondary syphilis that they have long occupied a foremost place in the symptomatology and diagnosis of the affection. The only other tissues which can compare with the skin in frequency of attack are the lymphatic tissues and perhaps the blood-vessels, but these are structures of universal distribution, taking their part in the local reactions in whatever organ these may be induced by the virus.

The special predilection of secondary syphilis for the skin may legitimately be extended to include the epiblast generally. The alimentary canal affords a striking instance of this truth. Lined throughout nearly its whole extent by epithelium of hypoblastic descent, its upper and lower extremities are formed by invaginations of epiblast known as the stomodaeum and proctodaeum. The mouth, tongue, and fauces, together with the lowermost part of the rectum, share the skin's extreme liability to the manifestations of secondary syphilis; the oesophagus, stomach, and intestines are to all intents and purposes wholly exempt. The epiblastic invaginations which go to form the external generative organs are another instance in point, and it is tempting to push the idea further and quote the eye and central nervous system, into both of which epiblastic elements largely enter, as illustrating the same principle. The mesoblast, however, is chiefly concerned in the formation of the iris and choroid, which are the main ocular structures liable to involvement in secondary syphilis, and the brain is more commonly affected at a later stage. Without pretending to enunciate any absolute law, we may, however, safely assert that on the whole the epiblastic tissues are the most susceptible to the syphilitic virus, and the hypoblastic tissues the least susceptible; the mesoblastic tissues, while occupying an intermediate position, approach the epiblastic rather than the hypoblastic tissues in susceptibility. Were one inclined to speculate as to the reasons for this, the suggestion arises that the parasite of syphilis has been evolved from a form which was primitively a genital saprophyte, and has hence ancestral predilections for squamous epithelium. When, in the course of its evolution, it began to acquire parasitic powers, the tissues to which it must first have become acclimatized were the mesoblastic structures of the cutis, and the lymphatic and haemal endothelium. To the hypoblast it must always have been a relative stranger.

The details as to the anatomical characters of the cutaneous eruptions of secondary syphilis belong to another section of this work. (Vol. IV.) They are epidermal and sub-epidermal in their ground-work, and the blood-vessels and perivascular lymphatics play an important part in their development. Their minute histology will be considered later. From the point of view of general pathology they may be regarded as local reactions induced by metastatic accumulations of the virus in a highly susceptible tissue. Their actual characters depend much upon their situation. On the dry surface of the skin they tend to be scaly : in moist situations, such as in the mouth and about the anus or vulva, they are covered by sodden epithelium, and constitute ‘ mucous tubercles ’ or ‘ condylomata ’. In the case of mucous membranes the inflammatory reaction may take on the characters of a diffuse acute catarrh, as in syphilitic rhinitis and the common sore throat of secondary syphilis.

Other general phenomena associated with the cutaneous eruptions may be briefly dismissed. There is a tendency to pigmentation of the rashes which may persist for some time after the rash itself has cleared up : while this is characteristic of syphilis it is by no means confined to that affection : many chronic inflammatory conditions of the skin are associated with pigmentary deposit. It is a common thing for the accessory structures of the skin to be affected : the lesions are sometimes localized about the hair-follicles (pilar syphilides), and the common diffuse alopecia of this stage of syphilis appears to be due to chronic inflammatory changes in the follicles. The nails, too, are apt to be affected by onychia and perionychia.

The Lymphatic System in Secondary Syphilis. The lymphangitis and indolent bubo which have already been described in connexion with the chancre are essentially phenomena belonging to the primary stage. They are local manifestations occurring before the clinical evidence of constitutional infection. During the secondary period, the predilection of the virus for lymphoid tissue is manifested by widely spread enlargements of the lymphatic glands. Such enlargements are rarely absent, and they occur as early in the secondary stage as the cutaneous eruptions. In the later stages they become more rare. For some unknown reason certain groups of glands are far more commonly affected than others; such are the anterior and posterior cervical glands, including the suboccipital group, also the cubital or epitrochlear glands. Although it is possible that these glandular enlargements are at times directly associated with, and secondary to, lesions elsewhere (e.g. the glands of the anterior cervical triangle in syphilitic sore throat), it is clear that in most cases they cannot be so explained. They usually bear no definite relation to the regions affected by the cutaneous eruptions: they may be present in the absence of any exanthem or other evident lesion: they may be absent in cases of severe cutaneous lesion. In general they probably represent the local reaction of a tissue for which the syphilitic virus has a marked affinity and in which it multiplies more readily than in most other tissues. These glandular enlargements in secondary syphilis run much the same course as the primary bubo: they are firm, painless, and indolent, lasting for weeks or months and tending ultimately to spontaneous resolution.

Far rarer than lymphadenitis in this stage of syphilis is a chronic and usually local lymphangitis, which may occur anywhere, but is most common on the male genital organs (Fournier). It is said that ulcerative processes over such foci may simulate a recurrence of the primary chancre.

In connexion with the lymphatic system may be noted the enlargement of the spleen which has not infrequently been observed in secondary syphilis. In the congenital disease this is a common phenomenon, but in acquired syphilis precise data are lacking as to the frequency of its occurrence. Post-mortem evidence is scanty, and the lesser degrees of enlargement of the spleen are apt to escape clinical observation. It is probable that some degree of splenic enlargement is a common thing in the secondary stage, and it has been observed early rather than late in this period.

Other Local Manifestations of Early Constitutional Syphilis. Although the blood-vessels may undoubtedly suffer in secondary syphilis their affections will most conveniently be considered together with those of the later stages.

We know very little of the pathology of most of the deeply-seated complications of this stage, for they rarely come under direct pathological observation. The locomotor system is very frequently affected—witness the common pains in the bones and joints—but the anatomical substratum of these pains is obscure. A true periostitis may indeed occur during the secondary stage, but incomparably less frequently than later. It is certain that the bone marrow is one of the seats of election of the syphilitic virus, for, with the spleen, lymphatic glands and testis, it is amongst the tissues giving the most constantly positive results on artificial inoculation; Neisser indeed considers the bone marrow the most constantly infective of all. The arthralgias of secondary syphilis are equally obscure, though serous exudation and reddening of the synovial membrane have been described.

The multiform nervous symptoms which have at times been observed in early constitutional syphilis assure us that the central nervous system is not exempt from attack at this stage, but we know next to nothing of the nature of the lesions produced, though we may infer that they are transitory.

The occasional occurrence of jaundice and of nephritis are indications of an almost equally vague nature. It is only when we come to the internal generative organs that the evidence becomes more precise. The influence of even early constitutional syphilis upon the reproductive function is a well-established clinical fact, and this in both sexes.

As regards the *male sex*, objective affections of the testicle are not common during the secondary stage of syphilis. An epididymitis may occur quite early in this stage, while towards its close, as it merges into the tertiary stage, a diffuse, non-gummatous orchitis is not very rare, and has been classed by different writers now as a late secondary, now as an early tertiary manifestation. Later, gummatous orchitis is common. But though there may be no evidence of testicular affection, animal experiment is at one with clinical experience in indicating the testis as one of the seats of election of the syphilitic virus. It has already been mentioned that the testis forms perhaps the only exception to the rule that inoculation, to be successful, must be by cutaneous channels. In experiments with apes and monkeys the testis, according to Neisser, is second only to the bone marrow in the frequency with which it harbours the virus. The *Spirochaete pallida* has so far never been demonstrated in semen, but the infectivity of this secretion in man has on two occasions been demonstrated by Finger and Landsteiner ; in one of these cases there was orchitis, in the other no evident testicular affection : Neisser on the contrary got negative results with human semen on seven occasions. The bearing of the above facts on the paternal inheritance of syphilis is obvious, and the clinical evidence for such inheritance from a syphilitic father, without known maternal infection, is very strong.

In the *female sex* interest centres upon what happens in pregnancy during the secondary stage of syphilis. It would be of interest to know whether the ovary shares the special susceptibility of the testis to the virus, but upon this point information is not as yet forthcoming. In the unimpregnated female the manifestations of secondary syphilis in the internal generative organs are of no special moment. Menstrual disturbance is not uncommon, as in other conditions associated with anaemia, but calls for no special remark. But when a syphilitic woman becomes pregnant, or a pregnant woman is infected with syphilis, phenomena of the greatest moment are apt to ensue. As Fournier has insisted, there is a reciprocal influence of the two conditions upon each other. Pregnancy exaggerates the local manifestations of secondary syphilis upon the genital organs : condylomata attain a magnitude rarely seen under other conditions. And secondary syphilis exercises an even more malign influence upon the course of pregnancy. In general it may be said that, taking as an index what happens to the foetus, it is a more serious thing for a syphilitic woman to become pregnant than for a pregnant woman to become syphilitic.

The matter is an extremely complicated one, and many points are as yet far from clear. The following are the main possibilities :—

1. A syphilitic father may beget a syphilitic child, the mother remaining free from evident signs of the disease.
2. A healthy woman may become pregnant and be infected with syphilis at the same time.
3. An already syphilitic woman may become pregnant.
4. A pregnant woman may become infected with syphilis, early or late in the course of her pregnancy.

The questions of chief importance concern the transmission of the disease to the child and the viability of such a child. As regards the channel of foetal infection there are three possibilities :—

(*a*) The fertilized ovum may be already syphilitic, as the result of the presence of the virus in the ovum or spermatozoon. At least in the case of the spermatozoon, there is good ground for belief in the occurrence of this mode of transmission, though it is probably not the common channel of hereditary syphilis.

(*b*) The placenta remaining healthy, the foetus may be infected by transference of the parasite from the maternal blood. This again is probably an uncommon mode of infection, though it seems clear that in some cases of congenital syphilis there is no evidence of placental disease.

(*c*) The placenta itself may be the seat of syphilitic disease. This appears the commonest channel of foetal infection.

Placental Syphilis. The question therefore arises, what constitutes evidence of syphilitic affection of the placenta? The presence of so-called ‘ infarcts ’ and of the small necrotic yellowish bodies which have been described as miliary gummata, but which seem rather to be aggregations of polynuclear leucocytes, is not now held to be irrefragable evidence of syphilis, common though these conditions are in the syphilitic placenta. Such appearances have been described even in the normal organ, and especially in the placenta of nephritis. It is hard to name any one criterion by which one can deem a placenta certainly syphilitic, apart from the occurrence of definite gumma, which is rare. One of the most constant features is an increase in the absolute weight of the placenta, and especially of its weight relatively to the foetus. The average normal placenta weighs some 600 grammes, and its weight should be to that of the foetus as 1 to 5½. In syphilis its absolute weight is habitually increased, while that of the foetus tends to be low from imperfect development, so that the relative weights are not uncommonly 1 to 3. The anatomical basis of this difference is held to be a hyperplasia of the chorionic villi, chiefly due to connective tissue increase about the blood-vessels in their axis, with or without secondary changes in the epithelium covering them. (See Plate XXXIII.) The effect of this is to narrow the maternal blood-spaces and so hinder the nutrition of the foetus : in the lesser degrees of such interference the weight of the foetus is diminished, while the higher degrees lead to its death. The affected region of the placenta may in part depend upon the channel of infection—maternal or foetal.

The viability of the foetus depends upon two factors—namely, the intensity of its infection, which alone may determine death, or the degree of interference with its nutrition secondarily due to placental disease, or more rarely to stenosis of the umbilical vessels from syphilitic affection of these.

I have entered into the matter here because it is during the secondary stage of syphilis that the influence upon the foetus is the most intense ; this influence seems to attain its maximum during the first year after infection, thenceforward gradually fading. Abundant evidence is forthcoming that a syphilitic mother may at first abort early, then later, then produce a living but syphilitic child, and finally healthy offspring.

If we consider the reasons for this special incidence of the virus upon the reproductive functions of syphilitic parents, it is not unreasonable to trace it to the necessities imposed upon an obligate parasite for the continuance of its race. Such an organism has two main prospects of transference from an infected to a healthy body. One is by immediate implantation on the surface of the latter, and in syphilis this is secured in high measure by what one might call the ‘ determination ’ of the virus to cutaneous structures during the early secondary period, whereby the parasite comes to be present in large numbers in the secretions from the surface lesions. The other is by passage from parent to offspring, and the parasite of syphilis has succeeded in exploiting this method of transfer to a degree which has hardly a parallel amongst infective diseases. It has done so by developing a special proclivity for the reproductive tissues. It is interesting, in this connexion, to note the determination of the spirochaete of the African form of relapsing fever to the ovary of the tick which has sucked infected blood, whereby the parasite is transferred to the next generation of tick as a preparation for further human infection. Here, however, the matter is complicated by the alternation of hosts.

The Later Phenomena of Constitutional Syphilis. It is customary to regard the course of acquired syphilis as divisible into three stages, known respectively as primary, secondary, and tertiary. Such a division is convenient and corresponds roughly with known facts, but it rests on clinical data only, and pathology cannot recognize these stages as sharply defined. From the clinical point of view the *primary* stage is that in which the infection appears to be purely local ; it comprises the period between the first objective manifestation of infection and the onset of constitutional symptoms. It has, however, been seen that the tardy bodily reactions against the progress of the infection render clinical evidence a very imperfect index of its true course. The primary stage is merely that in which it is apparently local. But even the clinical observer is baffled in attempting to draw a hard and fast line between the secondary and tertiary stages. In a general sort of way it may be said that the *secondary* stage is essentially one of exanthem and fever, and the *tertiary* stage one of infective granuloma. As a matter of fact, the disease gradually loses the characters of a specific fever, while those of an infective granuloma become more and more apparent, but there are intermediate manifestations which cannot certainly be placed in one rather than in the other stage.

Nevertheless the later stages of constitutional syphilis present phenomena of very different type from those of the earlier stage. As the acuteness of the infective process gradually wears out, the bodily reactions against it undergo a profound change. From a pathological point of view the differences between the early, or secondary, phenomena of constitutional infection, and the later, or tertiary ones, may be grouped under several headings, as follows :—

(1) Whereas the earlier stages show a general bodily reaction in the way of febrile movement and changes in the blood, these phenomena gradually subside and in a few months may disappear.

(2) The earlier stages are characterized by a high degree of infectivity: the secretions from the local lesions contain an active virus in large amount. In the later stages this is not so. It was long believed that material from gummata was entirely devoid of infective properties, and it is certain that such material contains the virus in minimal quantity and of feeble vitality. Nevertheless successful inoculations upon apes have been recorded in at least eight cases by different observers, though more frequently the result has been negative. In the successful cases the material has been unsoftened granuloma from a gumma not yet ulcerated or necrotic. In one of Hoffmann's successful cases the disease was of twenty-four years' duration. The spirochaete has also been demonstrated in gumma by four or five investigators, though in small numbers. The supposed difference in infectivity between secondary and tertiary lesions is thus a quantitative and not an absolute difference. With the recession of the early acute lesions of the constitutional disease the virus is already much less abundant; in the later stages it is with difficulty demonstrable. But the change is a gradual one. What is true of the virulence of the local lesions

is true also of the liability to transmission by inheritance, which slowly fades with the progress of the case.

(3) Allusion has already been made to the contrast between the tendency to symmetry of lesion in the earlier stages of constitutional syphilis and the habitual asymmetry of the later lesions. It is not difficult to understand why the chance accumulations of the parasite, as it becomes more scanty, should lack the bilateral distribution seen when it is more abundantly distributed throughout the body.

(4) But perhaps more striking than any other contrast between the early and late manifestations of constitutional syphilis, is that which concerns their course and local gravity. Whereas the ordinary secondary lesions show little or no tendency to local tissue-death, but clear up leaving behind them no permanent trace of their presence, the gummatous and other lesions of the tertiary stage are characterized by a very striking liability to early necrosis and ulceration, and almost always leave permanent and often serious local disfigurement. The contrast is an odd one for this reason, that one would expect the lesion in which the virus is abundant to be a graver one than that in which it is scanty and difficult of demonstration. Yet the reverse is the case. If the reason cannot be sought in the relative abundance and virulence of the infective agent, it must perforce lie in some alteration in the nature of the tissue reaction against the virus—a view which has been long and ably maintained by Neisser. In every syphilitic new formation of tissue, early or late, the process begins with the development of a granulomatous tissue of much the same structure. A comparison of the microscopic sections from the three stages of the disease, figured in Plates XVIII to XXI, will show the essential similarity of the histological changes in their early phases, especially with regard to the accumulations of plasma cells. But whereas, in the early reactions of the normal and unspoiled tissues against the parasite, the granulation tissue passes on to fibrosis and induration, and never or hardly ever to necrosis and ulceration, there is seen in the secondary lesions a tendency to spontaneous absorption of the accumulated cells, without fibrosis.

Later still there is a gradually increasing frailty or perishableness of the reactive new formation, whereby at an early stage it undergoes softening and necrosis, with extensive local tissue-destruction. This is the essence of a gumma. The contrast between the early and the late lesions of constitutional syphilis depends, as Neisser has insisted, on a change in the tissues, and not on any change in the virus. The virus is reduced in quantity, but not in quality, for where simian inoculation with tertiary material is successful, the result is identical with that produced with material from the earliest stages.

The profound change in the nature of the tissue-reaction has further been shown by the experiments of Finger and Landsteiner, who inoculated human beings already in the tertiary stage with large amounts of syphilitic virus. In those cases in which positive effects were produced, the lesion induced did not resemble a primary chancre, but is claimed to have been of the nature of a tertiary lesion—a tubercular or ulcerative syphilide.

The differences between the earlier and later stages of constitutional syphilis are thus seen to be of an important kind, and the terms 'secondary' and 'tertiary' may be usefully retained if we bear in mind that these stages are not separated by any hard and fast line, but imply a gradual change in the characters of the bodily reactions against the virus. As in the case of the secondary manifestations of syphilis, I propose to mention here only the more general characters of the tertiary lesions. Their detailed characters are described elsewhere in this work.

In a general way, it may be said that the tertiary stage is essentially that of the graver lesions of syphilis—those which too often terminate life, or leave behind them irreparable consequences. It is not an absolutely inevitable stage in the evolution of the disease. There can be no doubt that really adequate treatment in the earlier stages prevents its occurrence in all but the most exceptional cases. It has been noted clinically that tertiary manifestations more often follow in cases which have run a benign course in the earlier stages than in those in which the earlier symptoms have been severe, but it must be remembered that in the latter there is the more ground for prolonged early treatment. In practice the main condition which conduces to tertiary lesions is ineffectual early treatment. Nevertheless there appear to be exceptionally malignant types of the disease which are with difficulty kept in subjection by treatment, and it is also clear that the general bodily condition of the patient exercises an important influence on the occurrence of tertiary symptoms; bad hygienic conditions, alcoholism, any cause of ill health, local or general—all these are predisposing conditions. It is a question of the extinction of the virus in the body. Given good general health and adequate treatment this extinction is assured during the earlier constitutional stages and the patient is thenceforward safe. But in the absence of these conditions, the parasite is not actually destroyed: it is scotched but not killed, and the patient has 'latent' syphilis which, in spite of apparent good health, may at any time manifest itself by tertiary lesions.

As a rule the patient is in good general health during this latent stage, but from time to time a sudden and apparently spontaneous local growth of granulomatous new formation appears. This may occur but once, or may be repeated at irregular intervals. The granuloma may appear in any region of the body, though some tissues are more prone to it than others. The clinical phenomena are of the most varied description and cannot be considered here. As regards the date of outbreak, it can be said that tertiary lesions may appear at any date after infection from the first year onwards: in rare cases they may become manifest even while the secondary eruptions are still present. More usually there has been a period of quiescence and apparent health between the secondary and tertiary phenomena: the years of greatest incidence are the second and especially the third after infection. Fournier's figures, based on 4,400 cases of tertiary syphilis, show 188 cases during the first year after infection, 453 during the second, 471 during the third, and 388 during the fourth. The numbers fall in each succeeding year, at first rapidly, then more slowly, but the liability to tertiary manifestations remains for even fifty years and longer. The body as a whole has long ceased to react against a virus which has become minimal in amount and lurks inactive in some remote region, but from time to time, owing to conditions of which we know little or nothing, there is a local awakening of the parasite to transitory activity and a corresponding local tissue-reaction. And in severe cases of tertiary syphilis—those especially in which there is extensive necrosis and ulceration—the general health may suffer to a marked degree, a severe cachexia supervening as a result of the local lesions.

As regards the site of tertiary lesions, Fournier has analysed his 4,400 cases and shows the skin to be considerably first as to frequency of attack. Next in frequency comes the central nervous system, followed by the bones. Visceral syphilis, though far more common than in the secondary stage, is yet infrequent as compared with tertiary syphilis of the foregoing tissues.

The lesions themselves are commonly of the nature of the perishable granulomata known as ‘gummata’, or are fibrotic in character; the two may be combined—a reactive fibrosis taking place around a gumma. Arterial disease also takes an important share in the lesions of tertiary syphilis. It may be gummatous or fibrotic in its essential character, but its importance rests in the serious consequences to which it may lead.

A *gumma* may be defined as a localised new formation of granulation tissue, occurring during the later stages of constitutional syphilis, vascular in its early phases, but tending to early tissue death and caseation, with softening and, if superficial, ulceration. In its early stages a gumma is a firm, semi-translucent, greyish or greyish-red mass of tissue varying in size from that of a pin’s head to that of a walnut or larger. Later it becomes opaque, yellowish and caseous, with a liability to softening: it is frequently surrounded by a zone of fibrous tissue which, if the softened and necrotic tissue be absorbed or discharged, results in a dense fibrous scar.

A gumma is usually a localised new formation, but several such may develop simultaneously or successively. The gravity of the result naturally depends upon the tissue or organ involved, and scarcely any part of the body is exempt. In addition to the formation of local gummata there is a diffuse type of perishable granulomatous infiltration, which may attack the skin, but is also apt to affect the fauces, pharynx, and larynx. Here the tissues seem to melt away, as it were by a process of rapidly spreading ulceration ; the loss of substance may be very great and the cicatricial contraction of the tissues concerned in repair may lead to serious deformities.

The *fibrosis* seen in tertiary syphilis is largely a matter of repair, though it cannot well be dissociated from the syphilitic element in the case. Any area of necrotic tissue—an infarct, for instance, or a tuberculous mass—acts as a mild irritant upon the tissues around, and excites a reactive fibrosis by which it becomes shut off. The natural cure of tubercle rests largely on such successful encapsulation of the infective foci. In the case of a gumma it is hard to say how much of the surrounding fibrosis and scarring is directly due to the syphilitic virus, and how much to the non-specific action of a focus of dead tissue. There are, however, good reasons for the belief that much of the fibrosis is directly excited by the virus of syphilis. The plasma cell, which forms so conspicuous and constant a feature in the earlier stages of all syphilitic lesions, is by many held to be a precursor of the fibroblast. In the later stages of syphilis it fails in its development into fibrous tissue, and, in the area mainly affected, shares in the general tissue-death, though towards the outskirts fibrous tissue is formed. But there are certain lesions of advanced syphilis which are intrinsically fibrotic from the first. In the congenital disease, the typical affection of the liver is a pericellular cirrhosis which is purely fibrous, and, as a rule, shows no localised gummata. The indurative lung affection known as ‘ white hepatization ’, occasionally seen in new-born syphilitic infants, is also essentially a fibrosis. And in the acquired disease there are visceral affections such as interstitial myocarditis and orchitis, which are similarly fibrous changes. In the same category may be placed the sclerosing forms of osteitis which occur independently of gumma. Lastly, it may be added that certain of the fibrotic changes in late syphilis are traceable to arterial disease.

Vascular Affections in Syphilis. Although this article deals with the general pathology of syphilis, the affections of the vascular system must be mentioned in some detail on account of the wide-spread consequences to which they lead. There can be no doubt that, even from the earliest stages, the virus of syphilis exerts a special influence upon the blood-vessels. In the primary sore small arterioles may at times be found with thickened walls and a lumen narrowed by endothelial proliferation—a true endarteritis. (See Plate XXVI.) The distribution of the secondary lesions tends to follow the course of the small blood-vessels (see Plate XXI), and microscopic examination reveals not only endothelial changes within the vessels, but also and more strikingly a perivascular infiltration in the form of accumulations of plasma cells around the vessels and in the lymphatics which accompany them.

The main incidence of vascular disease in syphilis is, however, in the later stages. The heart itself suffers in more ways than one, though cardiac syphilis is relatively uncommon. It may be the seat of gumma, of fibrous myocarditis, of fibrotic changes associated with disease of the coronary arteries, and, much more rarely, of pericarditis and endocarditis. Syphilitic affections of the veins, although known to occur, are of relatively small importance. But arterial disease in tertiary syphilis is very common, and of the gravest consequence. It may occur in any artery, but, of the large arteries, the aorta, the cerebral, the pulmonary and the subclavian, femoral, and popliteal are the most frequently affected. The changes found are not sharply defined from those seen in ordinary endarteritis and atheroma and they may easily be confounded with these. Nevertheless, syphilitic disease of the arteries has certain predominant features. Of these, the most striking is that of an obliterative endarteritis—i.e. of a thickening of the intima so marked as more or less to occlude the lumen of the vessel. (See Plates XXII and XXIII.) Not every obliterative endarteritis is syphilitic: a very similar change is sometimes seen in tubercle—e.g. in the middle cerebral arteries in tuberculous meningitis—and indeed any chronic endarteritis may tend to obstruct the blood channel. But on the whole this feature is far more pronounced in arterial disease due to syphilis than in any other form of the affection, and the demonstration of obliterative arterial changes in or around a lesion, presumably syphilitic, offers strong confirmation of its truly syphilitic nature. The results of the obliterative process are necessarily serious, for not only is the blood supply by the affected vessel hindered in proportion to the degree of obstruction, but the vessel-walls themselves lose their contractility and become incapable of vasomotor response. Thus the nutrition of the parts supplied by the vessel may be impaired—even to the point of tissue-death. This may be brought about in a secondary fashion by the occurrence of thrombosis in the narrowed and diseased artery. Organs peculiarly prone to suffer from the effects of syphilitic arteritis are the brain and the heart; the cerebral and coronary arteries are amongst those commonly affected, and the organs in question are highly susceptible to interference with their blood supply.

Although obliterative changes are usually conspicuous in syphilitic arteritis, there are other features of the condition which are equally important. There is a tendency to a sort of callous induration of the arterial wall which in the smaller vessels is more diffuse, in the larger, and especially in the aorta, more patchy in its distribution. Much has been written as to the primary seat of this indurative change, and the following conclusions may be accepted. The primary and most characteristic changes in syphilitic arteritis are in the outer part of the tunica media and in the adventitia; the changes in the intima are secondary. In the middle and outer coats there appear accumulations of cells, chiefly around the vasa vasorum, which are themselves the seat of the syphilitic changes seen in affections of other tissues and organs. (See Plate XXIV.) Almost all the local manifestations of syphilis, it has been pointed out, begin in and about the blood-vessels, and arterial disease is no exception to the rule. The cell accumulations in the arterial wall rarely undergo necrotic change: small gummata in such situations are not indeed unknown, but gummatous arteritis is a rarity. The cell masses habitually pass on to fibrosis:

the adventitia becomes thickened and hard, and the boundary between it and the middle coat is obscured or lost. In the middle coat the muscular and elastic layers are here and there interrupted by fibrous foci : there is no new formation of elastic fibres, such as v. Hansemann has claimed to occur in ordinary arterio-sclerosis. The gaps in the elastic tissue are admirably seen in sections stained in orcein. (See Plate XXV.) These lesions necessarily impair the resisting powers of the arterial wall, and it is not improbable that the thickening of the intima is, at least in part, an effort at compensatory repair. Even so, the indurated and fibrotic arterial wall is far from possessing the strength and resilience of the normal vessel, and thus it comes about that syphilitic disease of the arteries, and notably of the aorta, is one of the most powerful causes disposing to aneurysm. It is also well established that syphilitic inflammation of the aorta tends especially to affect this vessel at its origin and to spread to the aortic valve. Hence it is that syphilis plays so important a part in the production of aortic valvular disease in young adults.

In all this there is nothing which absolutely distinguishes syphilitic arteritis from ordinary arterio-sclerosis. In the latter Thoma claims that the primary changes are in the middle coat, and that the thickening of the intima is secondary. Nevertheless we see in the subjects of syphilis arterial changes which, in non-syphilitics, occur at a much later age-period and which in certain respects are peculiar, e.g. in the commencement of the changes about the vasa vasorum, which themselves may show an arteritis, and in the tendency to indurative fibrosis, which has a much slighter tendency to fatty and calcareous degeneration than is seen in ordinary arterio-sclerosis and atheroma. It is probable that in any given case we see specific syphilitic changes intermingled with those common to all arterial degenerations. When once the integrity of the arterial wall is impaired, from whatever cause, the ordinary factors in defence are brought into play, but there can be no reasonable doubt that syphilis is an important cause of early arterial decay.

Even in congenital syphilis arterial changes are described, especially in the aorta, which resemble those seen in the acquired disease. It is doubtful, however, whether they so often lead to serious consequences.

Arterial disease in syphilis presents certain differences from the ordinary tertiary manifestations; it is more conspicuously indurative, with little or no tendency to softening and breaking down; it does not seem influenced in its course by the administration of potassium iodide. Hence there are some who class it, not with the true tertiary lesions but with the so-called 'parasyphilitic' affections.

Parasyphilitic Affections. It has long been recognized that syphilis acts as a predisposing cause of other diseases. A study of the lists of predisposing causes given in textbooks of medicine will show how large a share is credited to syphilis in this respect in diseases of the most diverse kind. How much of this evil repute is deserved it is difficult to say, but there are certain diseases in which it is beyond cavil that syphilis plays a part of overwhelming importance. The two most striking examples are the chronic degenerative affections of the nervous system—tabes and general paralysis of the insane. These diseases are not in themselves manifestations of syphilis; they are in no wise controlled by anti-syphilitic remedies; it is agreed by cautious observers that, in a certain small proportion of cases, preceding syphilis can be excluded with an approach to certainty. But the percentage of tabetics and general paralytics who present either a history or evidence of syphilis is so great as to make it certain that syphilis has much to do with the causation of the disease, though it may not be the inevitable antecedent. To quote actual figures: W. Erb, whose authority will not be disputed, writes, in 1904, that of 1,100 cases of tabes under his observation, 90 per cent. had a history of past chancre or secondary syphilis, while in only 3 per cent. could syphilis apparently be excluded. Of non-tabetic males over twenty-five years of age, only 21·5 per cent. had suffered from syphilis. Only a small number of syphilitics become tabetic: probably syphilis alone does not suffice as a cause. Evidence of similar character might be quoted as regards general paralysis of the insane; it may occur in those who have never suffered from syphilis, but the vast majority of its victims are syphilitics.

To express these facts the term 'parasyphilitic' has been applied to such affections, and it is a convenient one when used strictly in the sense above implied—i.e. to cover diseases not in themselves syphilitic, and occurring at times independently of syphilis, but in the great majority of cases affecting persons who have suffered from syphilis. It would appear that syphilis leaves behind it a tendency to certain changes, usually of a degenerative nature, which may become apparent long after all active signs of the disease have ceased. But it must be remembered that the subjects of parasyphilitic disease may still be in the stage of latent or indeed active syphilis. The term 'parasyphilitic' does not imply that the syphilis is necessarily a thing of the past: what has already been said as to the almost indefinite persistence of the virus negatives such a belief. And thus it comes about that such modern methods of research as the reaction of Wassermann, Neisser, and Brück, presently to be mentioned, frequently reveal the presence either of syphilitic products or syphilitic antibodies in the cerebro-spinal fluid of tabes or general paralysis.

Accessory Infections in Syphilis. In the preceding sketch of the course of syphilis, I have confined myself to the phenomena due to that disease alone, uncomplicated by the invasion of foreign micro-organisms. But, as a fact, such secondary invasions are not infrequent, and they may greatly modify the character and course of syphilitic lesions. Two conditions favour such secondary infections. The lesions of syphilis are largely surface lesions, and many of them tend to ulceration, or at least to a denudation of surface epithelium, which assists the ingress of other micro-organisms. It need hardly be said that the skin, the buccal cavity, and other mucous surfaces are teeming with bacteria, many of which are potentially parasitic. There is thus ample opportunity for the occurrence of secondary infections. There is a second reason why they are apt to occur—namely, a lowered resistance against infection on the part of the body generally, where health is gravely impaired as the result of the syphilitic infection itself or owing to bad hygienic conditions. It has been pointed out that as a rule the general health does not suffer much in syphilis. In an ordinary case the patient looks and feels in fair health, apart from his chancre, sore throat, or eruption: in correspondence with this maintenance of bodily health, his powers of resistance are not seriously impaired, and secondary infections are either absent or trivial and limited.

But in exceptional cases this is not so. The syphilitic infection may be of severe and malign type, and lead to serious ill-health and lowered resistance. Or the same effect may be traceable to previous illness, to malnutrition, or defective sanitary conditions, such as were at one time more common than at present. Under these circumstances secondary infections may assume a gravity out of all proportion to the syphilitic infection itself: widely spreading gangrenous and phagedaenic processes may supervene and may destroy life. The term 'malignant syphilis' has been used in such cases, but the question of the malignancy of syphilis is a complex one. As with other infective diseases, there doubtless exist 'strains' of the syphilitic virus which are more vigorous parasites than others, and capable of exciting more serious results in the body which they invade. Yet this factor probably plays an insignificant part in 'malignant' syphilis: the essential factor lies in the capacity for resistance presented by the body invaded.

This capacity for resistance may be racial or individual. In a country where syphilis has been endemic for centuries, what may be called a racial immunity becomes manifest: not only does the disease directly affect a certain percentage of the population, but, being eminently inheritable, it affects in lesser degree a large percentage of those who have not directly suffered from the primary disease. And thus in the course of centuries there comes about what has been called the 'syphilization' of the community, in the sense that almost every one has some ancestral taint, recent or remote, and, what is more important, a certain degree of inherited immunity. The truth of this might well escape remark were it not for the serious results which ensue when the disease is introduced into a country where it has not hitherto been present, and in which the racial immunity has not been developed. There is abundant historical evidence of the ravages caused by syphilis in a virgin race, even though the introduced disease may have been of no intrinsic severity. Herein, then, lies one cause of the 'malignancy' of syphilis.

Individual lack of resistance depends chiefly on preceding ill-health or insanitary surroundings, and influences not only the course of the syphilitic infection, but also the occurrence of secondary microbic invasion. Cases of malignant syphilis in this country are mostly of this nature and are now rarely seen. The reasons for their rarity are manifold. Apart from the 'syphilization' of the community and the consequent increasing mildness of the disease, early and accurate diagnosis and treatment, and improved sanitation, have done much to lessen the severity of its incidence on the individual.

Amongst the common secondary infections in syphilis a few may be noted as of especial importance: (1) The occurrence of *gonorrhoea* and of *soft sore* as concomitants of the primary infection has already been mentioned. These, with their shorter incubation period, are at first the conspicuous feature: later, the manifestations of true syphilis gradually disentangle themselves from these preliminary complications; (2) *suppurative affections*, mostly of staphylococcal origin, may complicate the surface lesions of secondary syphilis, or of other stages. It is clear that syphilis, *per se*, is not a suppurative affection; any accumulation of true pus—i.e., of polymorphonuclear leucocytes—is almost certainly due to secondary infection by pyogenic cocci. Pustular syphilides are thus to be explained. In the throat, much of the severe inflammation of syphilitic angina is probably of streptococcal origin, if we may judge by what is known of sore throat in other diseases; (3) the occurrence of *phagedaena* and *gangrene* in syphilis, while certainly associated with adventitious infection, is largely determined by lowered resistance. The process is akin to that sometimes seen in other infective diseases, e.g. noma and cancrum oris in debilitated children as a sequel of measles. We do not certainly know the actual bacterial agent which produces these progressive gangrenes: probably it is the combined work of a number of species, amongst which anaërobic bacilli are to be included. But it is clear that putrefactive organisms never attack healthy living tissues; a very greatly lowered resistance must occur before this is possible. Such depression of tissue vitality must be the essential condition of phagedaenic processes in syphilis; they are not confined to syphilis, and they are probably not the direct effect of the syphilitic virus; (4) lastly, it must be mentioned that *tubercle* is no uncommon complication of late syphilis. Many syphilitics die of pulmonary tuberculosis; much of what was at one time regarded as syphilis of the lung was probably in truth tubercle.

The General Pathology of Inherited Syphilis. The congenital form of the disease is the subject of a special section of this work, and I propose here to touch on a few general features only. The first striking difference between the congenital and acquired forms of syphilis lies in the absence of any known primary stage in the former. Whether the foetus be infected by way of the germinal elements or secondarily through the placenta, it would appear that the infection speedily becomes a general one without any evident local reaction at the portal of entry of the virus.

In the second place congenital syphilis commonly displays an intensity of infection almost without parallel in the acquired disease. The whole body is, as it were, saturated through and through with the virus. The spirochaete has been demonstrated in incredible numbers in the liver, spleen, and other organs: in acquired syphilis it is much more hard to find, and even in the primary sore it is less abundant than in the liver of the congenital affection. Even if this evidence be put on one side there remains another set of facts which cannot be gainsaid: by experimental inoculation of apes and monkeys it has been shown that the virus is abundantly present in congenital syphilis in the lungs, liver, kidney, ovary, and in the nasal secretion in 'snuffles'. Successful inoculations are the rule with such material, whereas in the acquired disease they are rarely if ever obtained. The abundance and diffuseness of the poison in inherited syphilis is further suggested by the severity and widely spread nature of its manifestations.

The explanation of the above features—viz. the absence of a primary stage and the severity of the infection—is probably to be sought not so much in any peculiarity in the channel of infection as in the low degree of resistance presented during antenatal life, and especially during the early stages of development of the ovum.

Given an abundance and a wide diffusion of the virus, the manifestations of inherited syphilis, to be discussed in detail in another section of this work, are quite naturally explained. They differ in degree rather than in kind from those of the acquired disease, though differences must of necessity arise where the virus attacks developing instead of fully formed tissues. Thus, for instance, we find disturbances of dentition and lesions of the epiphyses of long bones, which are absent when the disease is acquired in adult life. It is, however, remarkable that anything approaching a general arrest of development is uncommon. The lesions of what corresponds to the tertiary stage are as a rule much more symmetrical than in acquired syphilis, and arterial disease is less conspicuous and less grave in its results. On the other hand diffuse fibrotic changes are common in the viscera, notably in the liver, lung, spleen, and pancreas.

But while the lesions of hereditary syphilis are commonly severe, and manifest either at birth or within a few weeks after that event, cases are by no means rare in which syphilitic manifestations are delayed for years, sometimes even to adult life. Just as the acquired disease may remain latent for half a lifetime after the initial manifestations, so in the inherited form, in which the early symptoms are concealed from observation, tertiary manifestations may appear for the first time in adult life, and this in cases where no suspicion of a syphilitic taint had existed. This is one of the reasons that makes it almost impossible absolutely to exclude syphilis as the cause of any given lesion in later life. It must be assumed in such cases that for some reason the initial infection was a slight one, and that it had remained latent: the term ‘syphilis hereditaria tarda’ is applied to such cases.

CHAPTER XIV

THE GENERAL HISTOLOGY OF SYPHILIS

Such vague terms as ‘ plastic inflammation ’ or ‘ round-celled infiltration ’ no longer suffice the histologist. Modern cytological studies have enabled us to discriminate with some minuteness between the various cells concerned in the inflammatory process, even though we are not in all cases able to be certain as to their origin and fate. These cells are in part derived from the blood, in part from the fixed tissues.

Of the haemal leucocytes, the *polymorphonuclears*, which take so active a share in acute inflammations, play little or no part in the bodily reactions against the virus of syphilis. Some stray intruders may be seen in this as in other granulomata, but their importance seems small. Even smaller is the part taken by the circulatory eosinophil and basophil cells : even when cells with these staining reactions are demonstrable in a syphiloma, it may be doubted whether they are truly of haemal origin. The only leucocyte playing a really important part in chronic inflammation and granuloma formation is the *lymphocyte.* Lymphocytes may form the bulk of the small round cells constituting the infiltration. Since it has been shown that lymphocytes are not destitute of the power of amoeboid movement, there is no great difficulty in accepting their haemal origin, though some pathologists (e.g. Ribbert) regard them as derived from local proliferation of minute foci of lymphoid tissue. It is not yet quite clear what becomes of the lymphocytes in granulation tissue ; by many they are regarded as the parents of the plasma cells.

The tendency of a granuloma, if it does not undergo premature decay, is to undergo transformation into connective tissue, with a permanent system of blood-vessels and lymphatic spaces. It is not surprising, therefore, to find the fixed tissue elements belonging to these categories taking a prominent part in granulomatous formations. Proliferation of the local *connective tissue cells* and of the *endothelium* of the smaller blood-vessels and lymphatics is a constant feature.

There is one type of cell which plays so important a part in most granulomata, and in syphilis in particular, that it must be mentioned in some detail. It is the '*plasma cell*' of Unna. Since its recognition this cell has attained some notoriety in all doctrines concerning chronic inflammation. It is a cell considerably larger than the lymphocyte, with a granular protoplasm staining of a bright crimson colour by the method of staining introduced by Pappenheim (pyronin and methyl green, with differentiation in alcoholic resorcin): it is thus readily recognized. Its nature and origin have been the subject of some dispute: by most authorities it is believed to originate from the lymphocyte; others regard it as derived from the fixed connective-tissue cells. Pappenheim himself considers that the plasma cells and lymphocytes are not identical, though allied in their tissue genealogy. Both are derived ultimately from the connective tissues, but whereas the lymphocytes remain in the original round-cell stage, the plasma cells possess the power of transformation into spindle cells, and are identical with granulation cells. I can certainly affirm that in well-stained specimens of granulation tissue, it is possible to trace every gradation between the plasma cell and the fibroblast.

Only one other form of cell need be mentioned in this brief review of the elements in granuloma formation, namely the '*giant cell*'. In many granulomata, simple and infective, but most notably in tubercle, large multinucleate syncytia are seen, often of immense size, and containing at times hundreds of nuclei. In the case of tubercle there is much reason for regarding them as endothelial in origin, and this is very possibly true in other granulomata, though the subject is a contentious one. Giant cells are not uncommon in syphilomata.

Such is a short account of the more important cells which take part in chronic inflammatory processes generally. I have now to discuss the special characters of syphilitic granulomata, which present all the features of a chronic as opposed to an acute inflammatory reaction. In its earlier stages, at all events, the tissue reaction is that which we associate with the idea of 'repair'. The local response to infection with the syphilitic virus is above all a proliferation of the fixed tissue-elements, or at least of cells capable of development into permanent tissue. This, however, is true of the reaction in any simple wound or tissue lesion. In what respects is the response to syphilitic infection peculiar? The answer is one which must be considered under several headings.

(1) A marked feature of syphilomata is their vascularity. Even to the naked eye a chancre is a red and manifestly vascular structure, easily bleeding if roughly handled. Ehrmann has demonstrated in the primary sore an abundant new formation of capillary blood-vessels as one of the earliest stages of the lesion; the richness of the chancre in capillaries is at all times plain on careful microscopic examination. This is, of course, even more true of simple granulation tissue, but it is a character in which the lesions of syphilis present a strong contrast to those of tubercle, in which no such new development of blood-vessels ever occurs. A tubercle has, in fact, no vessels of its own.

A gumma, in its earlier stages, also shows very numerous capillaries; in the later stages these have vanished in the central caseous mass, though the vascularity may still be manifest at its periphery.

(2) Apart, however, from any new formation of blood-vessels, syphilitic granulomata constantly exhibit changes in the pre-existing vessels of the affected area which are in many respects peculiar. It has been asserted, and with some truth, that almost every syphilitic manifestation begins in or about the blood-vessels. Both endo- and peri-vascular inflammation are seen. As regards the latter, it has been noted that even in the primary sore the columns of infiltration which spread from the main mass into the tissues around, tend to follow the blood-vessels, as well as the lymphatic trunks. Much of this, however, may be in truth a perivascular lymphangitis. In the cutaneous lesions of secondary syphilis the perivascular infiltrations in the cutis are perhaps the most striking histological feature. In gumma the perivascular changes are less conspicuous.

As regards the endovascular affection, in the small vessels it is manifest chiefly as an endothelial hyperplasia, which may choke up the lumen. Thickened arterioles of minute size may at times be found in a primary chancre, their channels filled with rounded endothelial cells. (See Plate XXVI.) A similar condition prevails in the lesions of later syphilis. The larger blood-vessels are more especially affected in the tertiary stage, and this syphilitic endarteritis, which is much more than an endothelial hyperplasia, has already been described in sufficient detail.

(3) Syphilitic processes have also a close relation with the lymphatic vessels; peri- and endo-lymphangitis are commonly seen in syphilomata. But whereas the vascular changes are gravest and most pronounced in the later stages of the disease, the lymphatic changes are far more evident in the initial stages. The reason is that the lymphatic system constitutes the main portal of ingress of the syphilitic virus; when once constitutional infection is well established it is by the blood that the virus is disseminated. Thus it is that, in the primary sore, infiltration in and about the commencing lymphatic trunks is readily demonstrable; their channels are commonly blocked by endothelial proliferation and accumulations of leucocytes. A continuation of the process extends along the lymphatics to the bubo as already described.

(4) With regard to the individual types of cell taking part in the structure of syphilitic lesions, one stands out as pre-eminently characteristic. This is the plasma cell, found in abundance at all stages of the disease. In all the syphilomata which I have had the opportunity of examining in their early stages, provided that they have been appropriately hardened and stained, plasma cells have been abundant and conspicuous. To illustrate this I have caused coloured drawings to be prepared from sections of syphilitic products in the three main stages of the disease. (See Plates XVIII to XX.) One is from a primary chancre, one from a condyloma in the secondary period, while the third is from a young gumma of the skin. It will be seen that the histological features shown in the three drawings are so similar that it is difficult to discriminate between them.

Although an abundance of plasma cells is a striking and constant feature of young syphilitic lesions, it is not pathognomonic. The plasma cell is seen, and often in numbers, in simple chronic inflammations, as indeed might be expected if it is a precursor of the fibroblast. There is, however, a wide difference in this respect between syphilis and tubercle. A miliary tubercle consists mainly of endothelial elements ; the only plasma cells seen in connexion with it are a few scattered ones in the zone of reactive fibrosis at its extreme periphery, whereas in a miliary gumma they are thickly scattered through its whole substance. Nevertheless, there are forms of tubercle, especially in the skin, in which plasma cells are abundant : the trabeculae of cellular infiltration traversing the dermis in lupus may consist almost exclusively of these cells. This feature then, though habitual in syphilitic lesions, has no absolute diagnostic value.

A word may here be added as to the fate of the plasma cells in syphilis. Their natural destiny would appear to be transformation into fibroblasts and ultimately into fibrous tissue. In the indurative forms of syphilis this actually happens, but it is plainly not so in those lesions which clear up without permanent scarring. In the secondary eruptions, one may see under the microscope plasma cells in every stage of degeneration. In a gumma the plasma cells share in the central necrosis : only at the margin does fibrosis occur. Circumstances thus offer to the plasma cell three different fates. It may become organized into fixed tissue ; it may undergo atrophy without any general tissue-destruction ; it may share in a widespread tissue-death. And this is probably true of other tissue elements in syphilomata.

(5) The remaining tissue elements in the lesions of syphilis need detain us but a short time, as there is little about them distinctive of the disease.

The endothelium of the lymph spaces and vessels, and of the blood-vessels, undergoes great increase, but we do not find in syphilis that predominance of endothelial elements which is seen in a young tubercle. The latter essentially consists of a reticulum of so-called ‘ epithelioid ’ cells, of the endothelial nature of which there is not much question.

Nor do we find in syphilis that abundance of multinucleate syncytia which is so characteristic of tubercle. Giant cells do, indeed, occur, as in all chronic inflammatory lesions, but they are usually few in number.

As regards leucocytic infiltrations, these are mainly due to accumulations of lymphocytes, which are commonly present in abundance amongst the plasma cells.

In the later stages of any syphiloma, primary, secondary, or tertiary, fibroblasts may be conspicuous, and are probably derived, at least in part, from plasma cells.

The general characters of syphilitic lesions may thus be summed up as those of 'plastic inflammation'—i.e. a reaction, mainly on the part of the fixed tissues, which produces a granulation tissue, or granuloma, which should, under ordinary circumstances, pass on to permanent new tissue. But, as a rule, little new tissue is actually formed, and several reasons have been advanced for this, no one of which is wholly satisfactory. Doubtless the syphilitic virus itself exerts some deleterious influence upon the cells concerned in tissue-formation, but this cannot explain the wholesale tissue-death seen in gumma. For the virus becomes progressively less abundant as the disease advances, whereas necrosis is chiefly marked in tertiary lesions. Vascular obstruction, again, must hinder nutritive processes, and so promote atrophy and tissue-death : of the direct causes which check the permanent organization of syphilitic infiltrations, this is probably the most effective. But behind all this is the change in the nature of the tissue-reactions as the disease progresses—the 'Gewebs-Umstimmung' of Neisser, whereby the new formation of tissue becomes more and more frail and perishable.

It will now be convenient to sum up the foregoing facts in a short account of the actual histological changes seen in the different stages of syphilis.

The Primary Sore. Around the first manifestations of the initial lesion the epidermis shows an overgrowth of its inter-papillary processes, which extend deeply into the dermis. The lymph spaces, which in the epidermis lie between the individual cells, are distended, and cavities of some size may arise by dropsical disintegration of epithelial cells : such cavities are often seen occupied by leucocytes. Finally, when the chancre is well established, the epidermis may be removed by ulceration over the central area. Meanwhile, changes of greater complexity have been going on in the subjacent dermis, and it must be remembered that the virus has been introduced at the outset into an excoriation, so that the dermis is early affected. At the actual point of entry of the virus into the dermis, Ehrmann claims that the earliest recognizable changes are an abundant new formation of capillaries, and a dense infiltration with mononuclear leucocytes. From this centre the process invades the healthy tissues; the infiltration spreads amongst the clefts in the fibrous tissue, following especially the lymphatics and blood-vessels, and being everywhere accompanied or even preceded by a new formation of capillaries. There is thus a central area where the density of infiltration is greatest, surrounded by a zone of lesser, but still dense, infiltration, from which, again, columns of infiltration radiate into the normal tissues around. The infiltration consists essentially of plasma cells and lymphocytes, but is complicated by multiplication of the fixed connective tissue cells, and by endothelial proliferation on the part of the small blood-vessels and lymphatics in the form of an inflammation of the internal and external coats of these vessels. (See Plates XVIII and XXVI.) Giant cells are rarely seen in the infiltrate, but basophil cells may occur. The general impression given by a section from a primary sore is that of a dense granulation-tissue, but in the ultimate result the amount of tissue-destruction is slight, and there is little cicatricial scarring. A marked scar on the penis suggests the former existence of a soft-sore rather than of a true chancre.

Lymphangitis and Bubo. It has been already remarked that the lymphatic system constitutes the main channel of entry of the syphilitic virus. In correspondence with this, marked changes are found in the lymphatic trunks emerging from the chancre and in the regional lymphatic glands. The lymphatic trunks show a peri- and endo-lymphangitis, which is often nodular and irregular in its distribution. Frequently the lymphatics are actually blocked by endothelial proliferation and accumulations of leucocytes, and hence arise the local swellings known as ‘ bubonuli ’.

In such infarcted lymphatics may be found, in addition to endothelial cells and lymphocytes, fibrinous clots and groups of plasma cells. Ordinary syphilitic changes have also been described in the blood-vessels accompanying the lymphatics. It has been suggested, with some reason, that these obstructive changes in the lymphatics represent an attempt to bar the ingress of the parasite. If so, the attempt cannot be said to meet with the success which it deserves, for constitutional infection is practically always the sequel.

The histological changes in the primary bubo present nothing very distinctive. There is seen an indurative condition such as may be met with in chronic glandular irritation of other kinds. The enlarged lymphatic gland shows a manifest overgrowth of its stroma: there is a sclerosis of the connective-tissue framework so that the adenoid tissue is traversed by thick trabeculae of fibrous tissue. The endothelial elements of the framework show a marked hyperplasia; large rounded endothelial cells are a conspicuous feature, and may present more than one nucleus; even giant cells may occur. (See Plate XXVII.) In correspondence with this overgrowth of the stroma, the normal packing of the tissue with lymphocytes becomes relatively more sparse. Collections of cells are seen, however, in the lymph-paths and sinuses, and the blood-vessels and lymphatic channels frequently show obliterative changes. Fibroblasts and young connective tissue also develop around the glands. In all this there is nothing that can be regarded as actually distinctive of syphilis.

The Histology of Secondary Syphilis. Much attention has been paid to the histological changes seen in the various cutaneous syphilides. While the more fugitive eruptions, such as roseola, are chiefly due to capillary dilatation, most syphilides show a circumscribed exudation of cells in the papillae of the cutis, with changes of various kinds in the overlying epidermis. I can here allude to two general features only in these eruptions, but these are of such constancy that it is usually possible to determine the syphilitic nature of a skin eruption upon histological evidence. The first feature is the relation of the infiltration to the blood-vessels. It is essentially a patchy infiltration, lying immediately round the vessels, which it may surround like a mantle, or accompany at one side only. Secondary syphilides seem, indeed, governed in their distribution by the branching of vascular stems (Ehrmann). I have endeavoured to illustrate this feature of secondary syphilides in the coloured drawing (Plate XXI) which has been prepared from a section of typical syphilitic psoriasis. I owe this specimen, and many other sections of syphilitic skin affections, to the kindness of Mr. J. E. R. Macdonagh, to whom I am glad to acknowledge my debt.

The second constant feature of cutaneous syphilides lies in the abundance of plasma cells in the infiltration. Plasma cells are a common enough feature of chronic skin inflammations apart from syphilis : they are in no way diagnostic. But given a skin eruption in which a perivascular distribution of accumulations of plasma cells and lymphocytes is demonstrable, a strong case is made out for syphilis.

In addition to these characteristic changes in the dermis, there is commonly a marked proliferation of the epidermis, and especially of its interpapillary processes. In moist situations the thickened epidermis is swollen by imbibition of fluid, and may become a conspicuous feature, as in mucous tubercles. On the dry surface of the ordinary skin, the proliferated epithelium separates in scales. Ulceration and suppuration in secondary syphilides usually imply the action of adventitious infecting agents, mostly of staphylococci.

The skin lesions of secondary syphilis tend to clear up, leaving no permanent traces of their presence. During the recession of such lesions, the plasma cells may be seen undergoing atrophic changes. But although the syphilide may vanish to outward view, the microscope reveals for a long while the traces of its former presence. Hjelmman, in particular, has studied these residua, and finds remains of the infiltration persisting for at least a month after the apparent disappearance of the exanthem. Thus, perhaps, may be explained local relapses and the later occurrence of tertiary at the site of old secondary lesions. The pigmentation which at times persists is not altogether peculiar to syphilitic eruptions ; Ehrmann associates it with the presence of special connective tissue cells which he terms 'melanoblasts'.

Not rarely, infiltrations occur about the hair follicles and other cutaneous adnexa; thus arise the so-called 'syphilides pilaires', while the well-known syphilitic alopecia appears to result from a deep folliculitis with subsequent atrophy of the hair-bulb.

Our knowledge of the histology of secondary syphilitic manifestations, other than those of the skin, is exceedingly imperfect. Reference has already been made to what is known of their general character; they probably correspond in a general way to the affections of the skin—i.e., they are mainly characterized by perivascular infiltrations in which plasma cells play an important part.

The Histology of Tertiary Syphilis. It is customary to regard the formation of gummata and the process of fibrosis, which are the essential lesions of tertiary syphilis, as two distinct changes. This is not strictly the case. Both are new formations of connective tissue, and at their outset are similar; but whereas in fibrosis permanent fibrous tissue is formed, in gumma the cells tend to early necrosis and death; in the one case the reaction achieves its goal, in the other it fails. If this be so, it is no matter for surprise that the two processes are often seen in company—i.e. that failure occurs in one part of an affected area and success elsewhere. In most gummata there is a zone of successful repair at the margin.

Very young gummata are not easily obtained for examination except in infants dying soon after birth, but they may at times be excised from the skin in acquired syphilis; the specimen from which Plates XX and XXIX have been drawn was obtained in the latter way. There is really little to distinguish a gumma in this early stage from the tissue seen in a chancre or secondary syphilide. It is a local infiltration of the tissues with cells which are for the most part plasma-cells or lymphocytes. It is a highly vascular granuloma, with abundant new-formed capillaries, and though it is not always easy to demonstrate its commencement in relation to pre-existing vessels, there is reason for believing that this relation exists. It is claimed that the earliest changes are seen in the adventitia of arteries and veins ; in the liver of congenital syphilis, where these very early stages have chiefly been studied, the process seems to begin as a ‘ peri-pylephlebitis ’—i.e. an infiltration in the adventitia of branches of the vena portae. When the gumma is more fully developed, this early relationship to vessels is obscured, but now the arterioles, and to some extent the veins also, begin to exhibit the thickening of the intima which has been already alluded to as characteristic of syphilis, and which may usually be found, often to an extreme degree, in these vessels as they traverse the gumma or the tissue in its vicinity. (See Plates XX and XXVIII.) Groups of giant cells are not rarely met with in young gummata. (See Plate XXIX.) But at the time when a gumma comes under histological investigation it has commonly undergone extensive degenerative changes. In certain cases these are of a mucoid nature : there occur forms of gumma, most often in connexion with the bones, which are relatively poor in cellular elements and are gelatinous in character from mucoid transformation of their tissue. Much more frequently the degeneration is a caseous one. Either in the early round-cell stage, or later when fibrillation of the matrix has taken place, the tissues undergo necrosis and the cell outlines vanish. There is now seen in the central part of the mass a granular or obscurely fibrillar material, staining well with acid dyes such as eosin, but in which nuclear staining with basic dyes is absent, save in the broken-down chromatin-residua which alone remain, or in a few secondarily intruding leucocytes. (See Plate XXVIII.) The capillaries and other tissue-elements share in the general cell-death. Fat granules and other products of degeneration are present. Always, however, at the periphery of the mass a living capsule remains, cellular and vascular in the less advanced, dense and fibrotic in the more advanced forms ; the area of central necrosis merges gradually into this.

The necrotic portion of a gumma may finally undergo liquefaction and, if superficial, be discharged. Usually it is gradually absorbed, so that only the fibrotic area at its edge remains. The cicatricial contraction of this leads to puckering and scarring, whereby, in an organ such as the liver, a high degree of deformity may be produced. In this case the reactive fibrosis alone remains to tell the tale of former tissue destruction.

In other cases the necrotic changes are absent, and fibrosis forms the fundamental and sole lesion of tertiary syphilis. (See Plates XXX, XXXI, and XXXII.) This is perhaps commoner in the congenital than in the acquired form of the disease, but even in the latter it is by no means rare; indeed, in the heart and vascular system it forms the usual type of tertiary lesion. There are those who regard these purely fibrotic lesions, not only in the vessels but in the testis and other organs, as parasyphilitic in nature. Atrophy of the functional tissue elements is a common secondary consequence of fibrotic changes in the stroma.

Parasyphilitic Lesions. The histology of these need not detain us long. In tabes and general paralysis, which must be regarded as the types of such affections, the essential change is a degenerative one in certain definite regions of the nervous system. The degeneration primarily affects the nerve elements themselves, and is ultimately associated with a diffuse fibrosis due to overgrowth of the supporting connective-tissue stroma.

A word may be added here as to the occurrence of lardaceous disease in syphilis. It is notorious that this condition is habitually associated with chronic suppuration, and in many cases of tertiary syphilis lardaceous changes may be thus explained. But it is a well-established fact that, in syphilis, lardaceous disease may be set up without the occurrence of true suppuration. I know of no other condition, except syphilis, in which lardaceous disease occurs apart from suppurative affections. The experimental production of lardaceous change by Krawkow and others has enlarged our knowledge concerning it, but we are still far from understanding how the condition is produced. Syphilis is clearly an important cause of lardaceous disease: why it is so is uncertain.

CHAPTER XV

THE PROBLEMS OF IMMUNITY IN SYPHILIS

There is perhaps no infective disease in which the problems of immunity are so difficult of solution as in syphilis. In the past, reliance has necessarily been placed on clinical evidence only and although certain definite facts have thus been established, we have remained largely in the dark as to their real inwardness. Even inoculation experiments upon human beings have failed to settle these problems, for syphilis has always confronted us with a difficulty almost peculiar to itself—namely, its tendency to remain indefinitely latent in the body, still uncured. It has been impossible, on merely clinical evidence and even by human inoculation experiments, to decide whether cure was real or apparent, or whether apparent immunity did not truly represent, in many cases, the latent disease. But with accession of knowledge as to the causal agent, with the means of animal experiment which the discoveries of Metchnikoff and Roux have rendered possible, and with the application to syphilis of Bordet and Gengou's reaction by Wasserman, Neisser, and Bruck, paths of investigation have been opened up by which a solution of these problems may reasonably be anticipated. They are not yet solved, but they are defined, and in process of solution. I propose here to consider shortly what the problems are, and how far they have yet been cleared up.

Natural Immunity. Syphilis has always been regarded as an exclusively human disease. It is not known to occur naturally in any other animal species : innumerable attempts have been made to produce it in lower mammals, but never with unequivocal success till Metchnikoff and Roux inoculated the chimpanzee. The limits of inoculability are now fairly defined : below the monkeys there seems but one animal in which the syphilitic virus can take root and produce recognizable effect ; this is the rabbit, in which Hänsell's corneal inoculations, confirmed by several later observers, seem to have produced a specific keratitis and iritis truly due to the *Spirochaete pallida*. This, however, is merely an exceptional and isolated pathological observation; it is interesting that the rabbit, when inoculated in the cornea, may serve as a temporary host for the virus, but the fact has no bearing whatever on the origin and epidemiology of syphilis. The susceptibility of simians is of greater practical importance, because in them the induced disease has a much closer analogy with human syphilis, and is provoked with much greater readiness and certainty, so that inoculation of monkeys, and especially of anthropoid apes, constitutes a practically effective test as to the presence of the syphilitic virus. But even amongst simians the response to syphilitic inoculation bears a definite relation to the presumable genealogical affinity to man of the species inoculated. Many of the lower simians are immune. In the genera Macacus, Cynocephalus, and Cercopithecus only a primary lesion can be induced: true secondary phenomena do not occur, or are slight and doubtful, though by experimental means it is demonstrable that generalization of the virus actually takes place. Only in the anthropoid apes, and above all in the chimpanzee, is the primary sore followed by true secondary lesions, comparable with those seen in man. And even in the chimpanzee tertiary lesions are so far unrecorded, though this may be due to the fact that these apes do not live long enough in captivity to afford a fair test.

The inference from these facts is sufficiently clear. It is that syphilis is essentially a human disease, as has always been believed. It must have originated in the human species, and still has this limitation, under natural conditions. That it can be transmitted to the ape, in lesser degree to certain monkeys, and even in a manner to the rabbit, proves only that the chemical and physical conditions offered by the tissues of such animals, in proportion to their affinity with man, permit of the more or less limited growth of a parasite which is still essentially a human parasite. Lower mammals present in the main a natural immunity: their tissues are adverse to the development of the parasite—so adverse that no local reaction against it is needful.

Acquired Immunity. Allusion has already been made to the mitigation, in regard to severity of symptoms, which seems to occur in countries where syphilis has long prevailed. This cannot be due to any inherent weakening of the virus itself, for, introduced into a new country, the ravages of the disease may become at once of great severity. It must be traced, as has been already suggested, to a change in the resistance of the population as a whole—a partial racial immunity, as it were, which has arisen where some degree of inherited taint prevails, with greater or less remoteness, in almost every family.

But the question which here chiefly concerns us is the immunity acquired by the individual as the result of an attack of syphilis. It is a well-known fact that a person who has suffered from syphilis is little liable to contract it a second time, but it must not be inferred from this that a true immunity is necessarily present. For syphilis is peculiar amongst infective diseases in the long years during which it may remain latent, and in the majority of cases the patient is apparently immune only because he is still syphilitic. This, as Neisser has justly urged, is not true immunity: the most that can be said of such a case is that the skin is relatively insusceptible to the access of new virus.

The very careful investigations of Finger and Landsteiner have shown that the insensitiveness of the skin to re-inoculation, in syphilitic subjects, is not so complete as has been supposed. The ‘ immunity ’ is not absolute, though it is far-reaching. They find that re-inoculation is successful in proportion to its proximity, in point of time, to the primary inoculation. If general infection is not yet complete, a typical chancre can be produced, but from the time when constitutional symptoms appear it becomes progressively more difficult to succeed. During the secondary period the result has some resemblance to a secondary papule, while in the tertiary stage ulcerative or tubercular syphilides are produced, resembling tertiary lesions. And to produce any effect at all in these later stages, large amounts of the virus must be introduced.

It is probable that many so-called second attacks of syphilis are of the nature indicated by the experiments of Finger and

Landsteiner—i.e. re-exposure to infection has led to a local effect which is not a true primary sore but a manifestation corresponding in character with the stage of the disease at which the patient has arrived. Again, ulcerative processes over foci of syphilitic lymphangitis on the penis, may in rare cases simulate a recrudescence of the primary sore.

There is nevertheless evidence that true second attacks of syphilis may at times occur. By a true second attack should be meant the occurrence, twice in a patient's life, of a primary sore followed by secondary symptoms, and if this definition be accepted, the phenomenon must be admitted to be of extreme rarity. As Neisser points out, it means not only that the patient has been completely cured of his first attack, but that his tissues have so returned to the normal as to react to the syphilitic virus like those of an intact person, and, it may be added further, that he has lost any immunity which may have been conferred by his first attack.

It will be apparent, from the above considerations, that it is a matter of extreme difficulty to decide on the degree of true immunity conveyed by an attack of syphilis. True immunity can only be present when the disease no longer exists, and we have no body of evidence to show to what extent such immunity is present in cured syphilitics. It is probable that an attack does leave some degree of immunity; but the rare occurrence of second attacks proves that it is not always perfect; and there is a strong presumption that much of what passes for immunity depends on still latent syphilis. This is one of the problems which still await final solution.

Other problems are presented by inherited syphilis. It is a well-established fact, formulated in *Baumes*' or *Colles's Law*, that where a mother, herself apparently free from syphilis, bears a child syphilitic by inheritance from the father—a not infrequent occurrence—she is immune and cannot be infected by her child, although such a child may readily infect another person, such as a wet-nurse. Another well-known fact formulated in *Profeta's Law* is that, where a non-syphilitic child is borne by a syphilitic mother, the child exhibits a similar immunity. These laws are the reciprocal expressions of a single fact, that, though the disease has itself to all appearance failed to be transmitted in one or the other direction through the placental circulation, an apparent immunity has been so transmitted.

That the facts are as just stated is not a matter which can be disputed, but we do not yet understand the nature of the immunity which is presented by the two cases cited; indeed it is not certain whether it is a true immunity or a latent infection. Something has traversed the placental circulation, from mother to foetus, or foetus to mother, as the case may be. This 'something' may be the syphilitic virus itself, in which case the immunity is apparent only, and what is really present is a latent infection. Or it may be, not the actual virus, but toxins or other chemical substances (antigens) derived from the virus, and capable of exciting the formation of antibodies in the uninfected individual; if so, the phenomenon is of the nature of an active immunity. A third possibility is that antibodies are formed only in the tissues of the infected subject, but are transmitted through the placenta to the uninfected subject: if so, there is a true immunity, but it is of the passive variety. It is not yet settled which of these three conjectures represents the truth, nor are we certain how lasting is the apparent immunity stated by the laws of Colles and Profeta; it is probably transitory.

Such are some of the chief problems concerning immunity in syphilis. In the past there has been no means of solving them in the only way in which a lasting solution is possible, namely, by actual experiment. But now more than one way has been opened out by which we may hope for definite answers to all such questions in the near future. The distinctions between a latent and a cured syphilis, or between a latent syphilis and a true immunity, may in time be finally settled by inoculation experiments upon apes—a costly method, it is true, but not too costly in view of the importance of the issue. There is, however, another method of investigation, too recently introduced for us yet to judge of its full possibilities, but promising information of such extraordinary value that it must be explained in some detail. I refer to the reaction of Wassermann, Neisser, and Bruck.

Serum-diagnosis. The reaction in question is based on a principle first published by Bordet and Gengou in 1901. It is well known that the serum of an animal which has been immunized with the red blood corpuscles of another species acquires the power of haemolysing these corpuscles. It is established that the haemolysing agent is of dual nature. The acquisition of the haemolytic power depends on the development of an ‘immune-body’ or ‘amboceptor’, which is thermo-stable (i.e. can resist a temperature of 55° C.). The other active agent in the haemolysis is a thermo-labile ‘complement’, or ferment-like substance, normally present in the serum, but destroyed at the above temperature. If the serum of the immunized animal be heated for half an hour to 55° C., its haemolysing power is lost, because the natural complement is destroyed, though the immune body is untouched: such a heated serum is said to be ‘inactivated’, but it can be ‘activated’ again by the addition of the serum of a normal animal, since this contains the natural complement. The serum of the normal animal alone, in spite of its complement, cannot cause haemolysis because no immune body is present: the complement can produce its effects only through the intermediation of the immune body. If we have simultaneously present (1) the red corpuscles of a given animal, (2) the inactivated serum of another species of animal which has been immunized against the corpuscles of the first animal and (3) fresh complement in the form of the normal unheated serum, we have what is called a ‘complete haemolytic system’.

What is true of haemolysis is true also of bacteriolysis, in which also immune-body and complement are concerned: similar facts seem, indeed, to hold good for most reactions between ‘antigens’ and ‘antibodies’. (The term ‘antigens’ is applied to those substances, be they bacteria or their products or other foreign cells or material, which evoke the formation of antibodies.)

Bordet and Gengou showed that, in an otherwise complete haemolytic system, haemolysis was prevented if the complement had first been incubated in the presence of cholera vibrios together with cholera-immune serum. The explanation was that the bacteria and the antibody, by their interaction, abstracted the complement and so rendered the haemolytic system incomplete. Later they extended this to other microbes and their antibodies, e.g. plague, and the phenomenon is now a well recognized one going by the name of *deviation of the complement.* Wassermann has extended the scope of the reaction, proving that it can occur with the crude infective material in cases where the microbe cannot be cultivated in the pure state. The paper in which Wassermann, Neisser, and Bruck first published their observations on complement deviation in syphilis, and established the possibility of serum diagnosis in this disease, appeared in 1906. The method has since been employed by other observers, and no doubt can now be entertained as to its practicability and value.

The details as to the method employed are as follows : The haemolytic system which Wassermann and his colleagues used was composed of (1) the red corpuscles of the sheep, washed and suspended in normal saline solution ; (2) inactivated serum from a rabbit highly immunized against sheep's corpuscles ; (3) fresh guinea-pig's serum as complement. In any experiment the activity of this admixture must be tested as a control. The syphilitic antigen consists of an extract of any virulent syphilitic material obtainable : this may be primary chancre, or condylomata, or, best of all, fresh viscera from a case of congenital syphilis, preferably liver, since in this the virus is most abundant. The extract is made, so far as possible with aseptic precautions, in normal saline solution containing 0·5 % carbolic acid, four parts of the fluid being used for one part of the tissue. The tissue is first ground in a mortar, then shaken with the fluid for twenty-four hours, and finally centrifuged. The resulting clear extract contains the antigen (4). The syphilitic antibodies (5) consist of known antisyphilitic substances, such as the inactivated serum of monkeys previously immunized by large doses of syphilitic material. If now a mixture be made of syphilitic antigen and antibody (4 and 5) with (3) fresh guinea-pig's serum, and incubated at body temperature for three quarters of an hour, and if then the corpuscles and haemolytic serum (1 and 2) be added, and the whole be further incubated for two hours, no haemolysis is found to occur. The interaction between the syphilitic antigen and antibody has used up the complement and the haemolytic system is rendered incomplete.

Such is the reaction with known syphilitic antigen and antibody, and it is plain that the method can be used as a test to determine the presence of either of these in unknown material. If, for example, one has, under (4), known and certain syphilitic antigen, and the unknown material be used as (5), the reaction can determine whether or not antibody is present in this material. Conversely if, under (5), one has known antibody the test becomes one as to the presence or absence of antigen in the unknown material used as (4). A positive reaction (i.e. inhibition of haemolysis) answers either question in the affirmative, while if haemolysis proceeds unchecked it may be concluded that no antibody (or antigen, as the case may be) is present in the material tested. More than this, by employing a standard antigen in various dilutions, it seems possible to determine not only the presence, but even the approximate amount, of antibody in any given serum or extract.

The principle of the reaction will be apparent from the above short account, but it must be added that the fallacies which may beset it are numerous, and require a variety of control tests to exclude them. Normal serum should be employed as a control to the suspected serum, and normal tissue extract as a control to the extracts of syphilitic tissue. The titre of the haemolytic amboceptor must be known, and the dose should be double that capable of causing complete haemolysis of the volume of corpuscles employed.

Neisser states that he and his colleagues have always been able to demonstrate antigen in material certainly syphilitic, and never in material which was certainly non-syphilitic (e.g. the tissues of normal apes). They have tested 262 cases of human syphilis, manifest or latent, and have obtained evidence of the presence of either antigen or antibody in 65·5 % of the cases (70 % in manifest, 58 % in latent syphilis). A positive reaction thus comes to be of diagnostic value in a doubtful case: a positive antigen-reaction implies the existence of active virus in the body: a positive antibody-reaction means a past infection which may still be latent or may have been replaced by an immunity. A negative reaction allows of no certain conclusion.

For purposes of practical diagnosis, more attention has been paid to the reaction for antibody than that for antigen. The blood is the only material which can conveniently be examined in clinical practice, and even in cases of evident syphilis antigen may be totally undemonstrable therein, just as, again and again, it may be found lacking in infective properties. Antibody, on the other hand, is more constantly to be found in the blood.

On the strength of some 1,000 cases in which the serum reaction has been tested, Wassermann considers that fairly consistent results have been obtained. The reaction is invariably absent in non-syphilitic persons, and it is positive in about 85 % of syphilitics. The percentage of syphilitics giving the reaction varies with the stage of the disease: no result may be obtained in the first six or eight weeks, and the secondary stage is that in which a positive result is most constant, though the percentage is nearly as high in the tertiary stage. Treatment, too, probably exercises an influence on the reaction.

The highest value of the reaction is not, however, in manifest syphilis but in obscure cases—those in which syphilis has never been diagnosed or treated. In parasyphilitic affections the reaction is often positive. In the cerebro-spinal fluid of general paralysis of the insane Wassermann and Plaut obtained a positive result in 78 % of forty-one specimens examined. The blood also commonly gives a positive reaction in this disease, and also in tabes dorsalis, but in the latter the cerebro-spinal fluid is, for some unexplained reason, more often negative.

The reaction may very possibly be of value as an indication for treatment. It is probable that in cases of old syphilis the amount of antibody present affords an index of latency or cure. Experience is not yet sufficiently abundant to determine how far the reaction will prove of utility in this respect.

It will be seen, from what has been said, that this reaction of Wassermann, Neisser, and Bruck promises to be of singular value in the solution of immunity-problems in syphilis, since it affords information of a kind which can be obtained in scarcely any other way. We may, indeed, await the settling of these doubtful questions in the near future with some confidence.

Artificial Immunity. By this is here to be understood a true immunity, such as can be produced against various bacterial infections, not a therapeutical prophylaxis with local ointments. Numerous attempts have been made to immunize human beings and apes, but so far with little or no success. Amongst the means which have been tried are injections with the serum of animals naturally immune against syphilis, of animals which had previously been treated with mercury, of animals syphilized with material from human cases of the disease, and lastly injections of human serum from syphilitics in all stages. No satisfactory protection seems to be afforded by any of these procedures, and the outlook for serum therapy in syphilis is at present far from encouraging.

There remains, however, a somewhat more hopeful possibility, to wit, the employment of an attenuated virus as a vaccine. Just as the virus of small-pox, modified by bovine transmission, can be employed with safety as a prophylactic against that disease, so it may prove possible to attenuate the virus of the great pox, by passage through a relatively insusceptible animal, to a point at which it may be used without risk for human inoculation, while still conferring an immunity against the virulent disease. The facts as to the results of animal inoculation which have been set forth in this article point to some of the lower monkeys as the most likely agents for such an attenuation of the virus, and Metchnikoff has already brought forward some evidence, not indeed conclusive, but pointing in this direction. One of the attendants upon his monkeys developed two small ulcers in succession upon the lower lip. These soon healed, but material from one of them produced syphilis when inoculated upon a Macacus. The man was not treated for syphilis, yet he developed no further sign of the disease, and Metchnikoff regards the case as one in which a weakened virus, derived in some accidental manner from a monkey, produced a localised and trivial human lesion only. Metchnikoff further inoculated an old man of 79 years, who voluntarily offered himself for the experiment, with a virus which had been passed five times through monkeys. Papules resulted, which slowly disappeared, and no further phenomena of syphilis occurred during the succeeding twelve months. A chimpanzee and a Macacus, inoculated at the same time with the same virus, developed typical primary syphilis. These observations are highly suggestive, though too few to establish any far-reaching conclusion. Nevertheless, along some such path the most hopeful prospect of inducing a true immunity against syphilis would seem to lie.

F. W. Andrewes

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The bibliography of Syphilis is enormous: the following short list of authorities contains only those works which I have chiefly had occasion to consult in the preparation of the foregoing article. I must, in particular, acknowledge my debt to Herxheimer's laborious review of the subject in the eleventh volume of Lubarsch and Ostertag's 'Ergebnisse', to Neisser's masterly address at the Berne Congress of the German Dermatological Society, and to Fournier's well-known treatise.

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Plate XVIII.

Section of the granulomatous tissue in a recent, but fully developed, primary chancre of the labium majus. Stained with pyronin and methyl green to show the abundance of Unna's 'plasma cells', which are distinguished by the crimson granulations in their protoplasm. × 500.

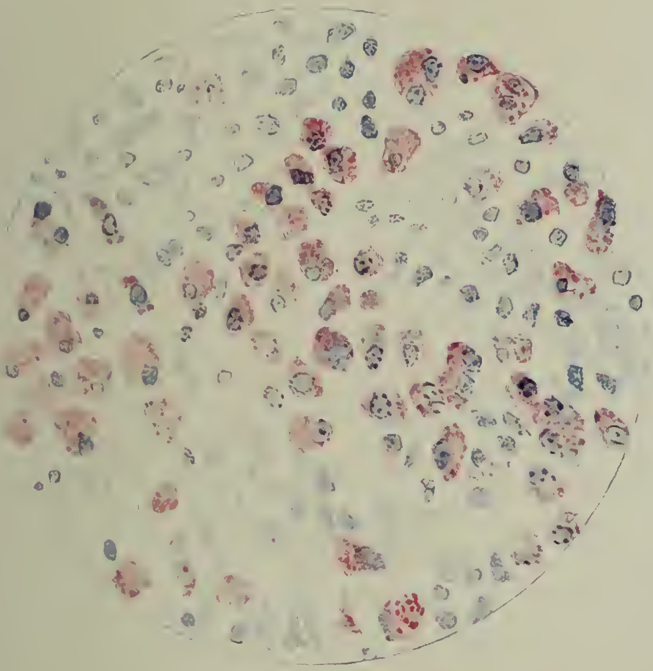


Plate XIX.

Section of a syphilitic condyloma, stained by Pappenheim's method to show the dense infiltration of the cutis with plasma cells, the protoplasm of which is stained crimson. Two interpapillary processes of the epidermis are seen. × 200.

(*From a preparation by Mr. J. E. R. Macdonagh.*)

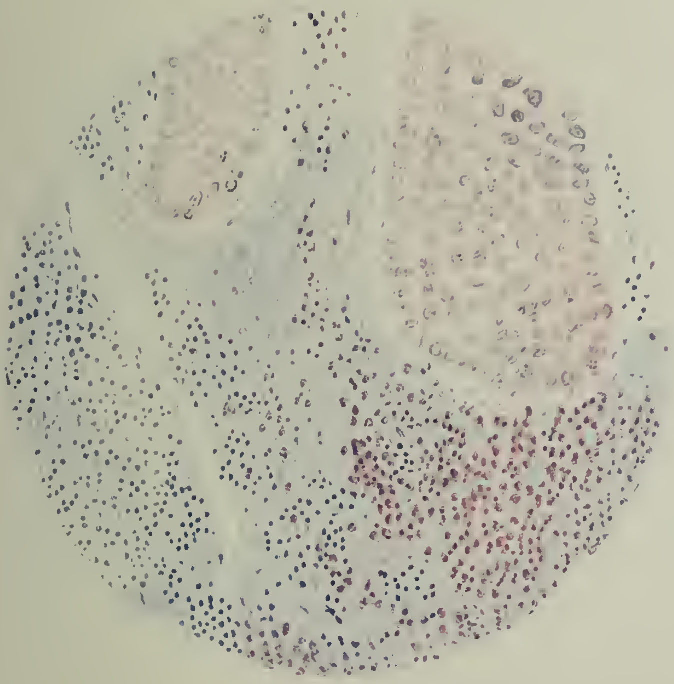


Plate XX.

From a section through a small recent gumma of the skin, stained by Pappenheim's method to show the numerous plasma cells. The plasma cells are here seen grouped round a small blood-vessel. × 500.

(*From a preparation by Mr. J. E. R. Macdonagh.*)

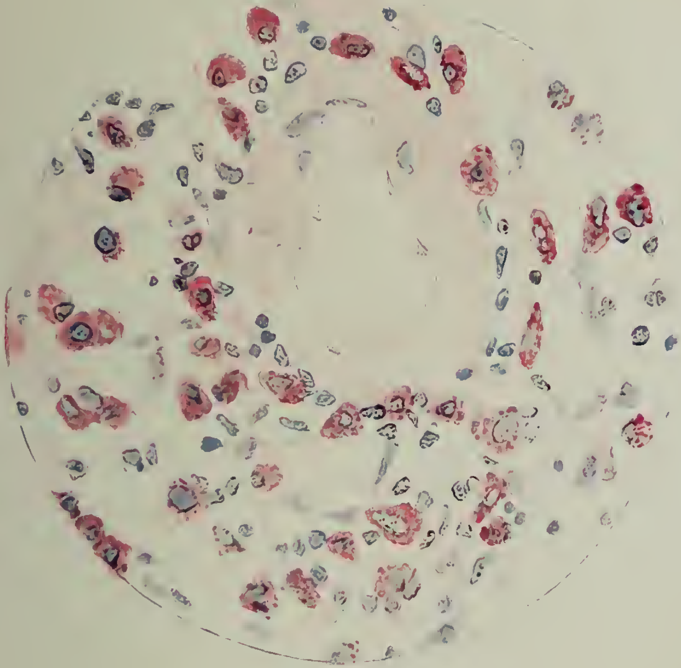
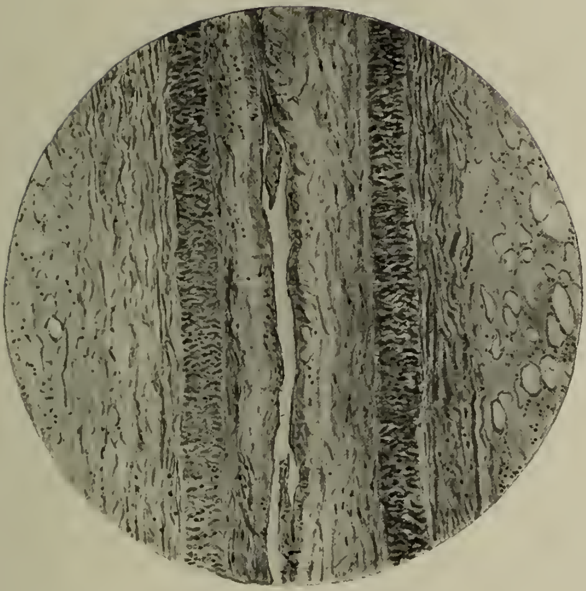


Plate XXI.

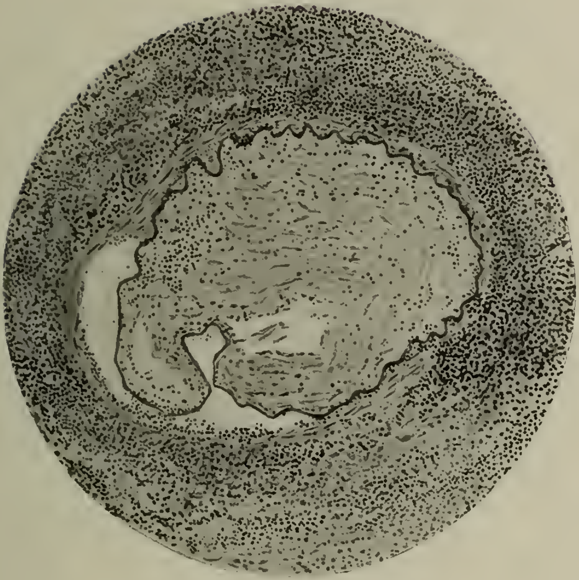
Section through a squamous secondary syphilide (syphilitic psoriasis), stained by Pappenheim's method. The figure is designed to give an impressionist view of the distribution of the plasma cells. They occur in patches in the dermis because they are grouped round the blood-vessels, but these vessels are scarcely indicated in the figure. × 100.

(*From a preparation by Mr. J. E. R. Macdonagh.*)



Longitudinal section of a small branch of one of the Coronary Arteries lying in the visceral pericardium over a gumma of the heart wall. It shows an obliterative endarteritis which has reduced the lumen of the vessel to a narrow chink. × 150.

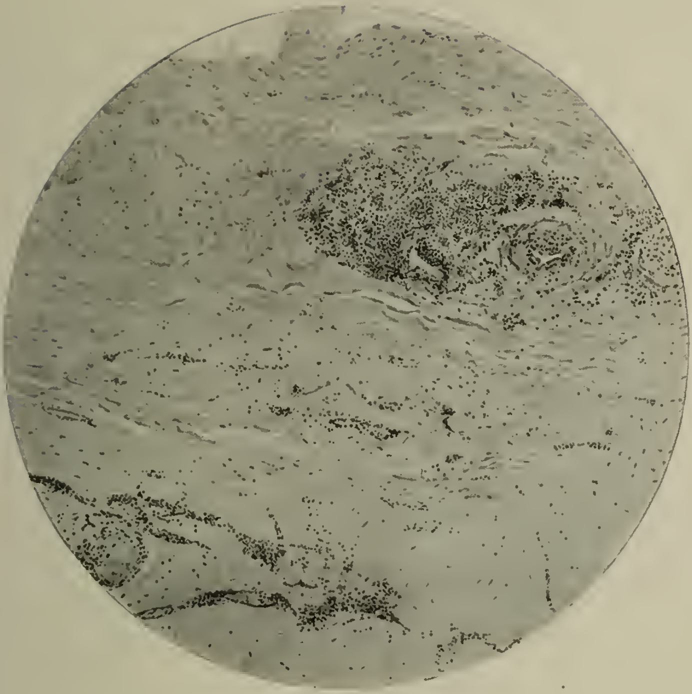
PLATE XXIII



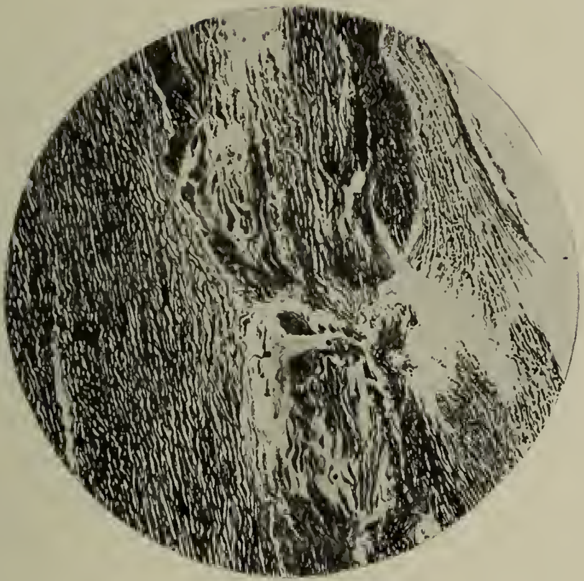
Transverse section of a small cerebral artery, included in a gumma of the brain. The lumen is almost occluded by an obliterative endarteritis. The internal elastic lamina has in one place become detached from the rest of the tunica media. × 150.

From a preparation lent by Dr. J. H. Drysdale.

PLATE XXIV

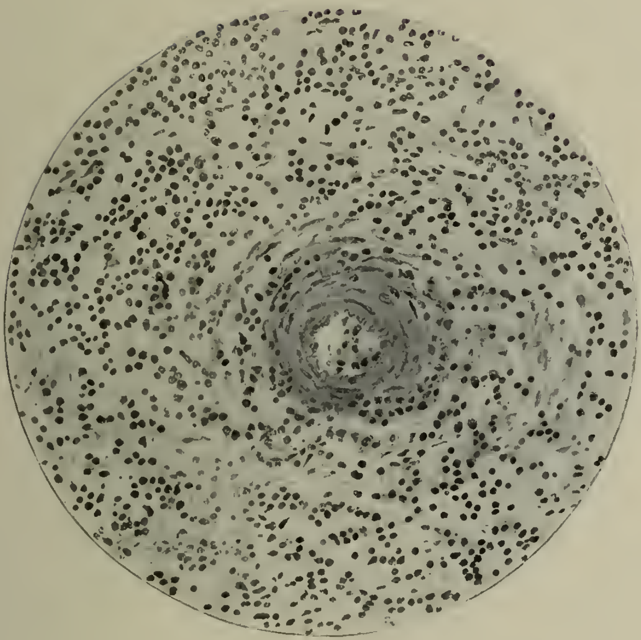


Section taken through the tunica adventitia of an aorta. The subject was a young man known to be syphilitic, and the cause of death was acute valvular disease; there was extensive implication of all three coats of the aorta. The section shows local areas of inflammatory infiltration in connexion with vessels and nerves in the adventitia and outer layers of the media. The large area of infiltration lies in the adventitia, and is in connexion with one of the vasa-vasorum, which itself shows typical syphilitic endarteritis. The following plate, showing the gaps in the elastic tissue of the media, is from the same aorta. × 100.



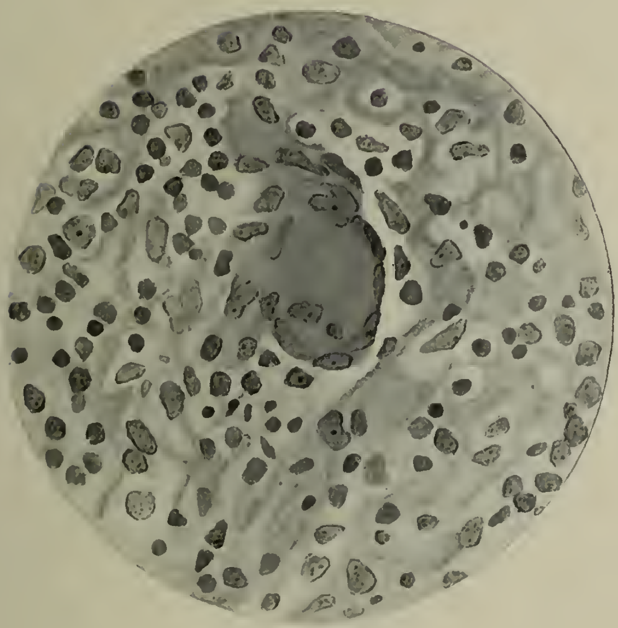
Section through the middle coat of the aorta of a young man who died of aortic valvular disease due to syphilis. The preparation is stained with orcein, and the elastic tissue is alone visible. The gaps and irregularities in the elastic network indicate the breaking up of the middle coat by syphilitic infiltrations. × 100.

PLATE XXVI



From a section through a primary chancre of the labium majus, to show the arterial changes which may be present even at this stage. An arteriole is seen cut across transversely; its walls are thickened, and the lumen is occupied by proliferated endothelial cells. The remainder of the section shows the granulomatous tissue forming the bulk of the chancre. × 400.

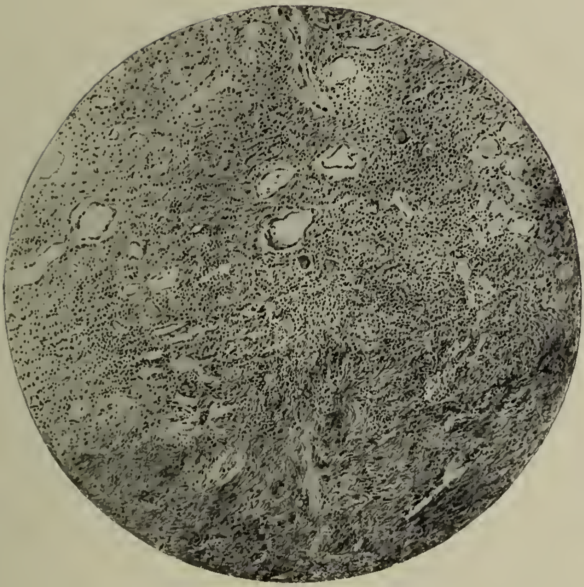
PLATE XXVII



From a section of an indolent bubo of the epitrochlear lymphatic gland, consequent on primary syphilitic infection of the index-finger. The gland, which was as large as a chestnut, was excised about the time of the appearance of the secondary eruption. It shows overgrowth of the stroma and marked endothelial proliferation, with a well-marked giant cell in the centre of the field. ×500.

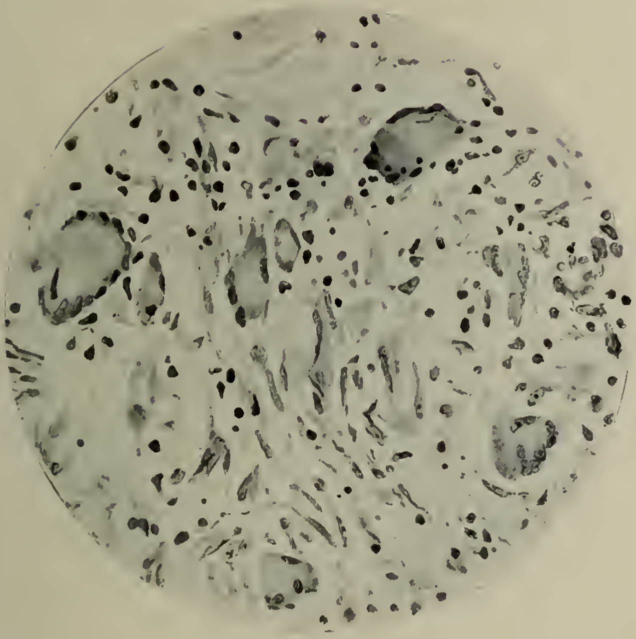
From a specimen lent by Dr. F. Parkes Weber.

Plate XXVIII



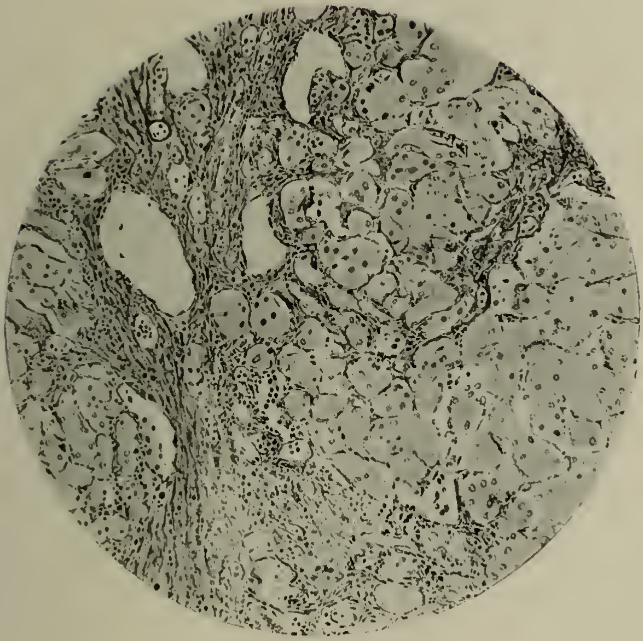
From a section through the edge of a gumma of the brain. At the lower side the tissue is caseous and fibrillated, but the greater part of the figure shows a cellular granulomatous tissue in which numerous blood-vessels are present. × 100.

PLATE XXIX



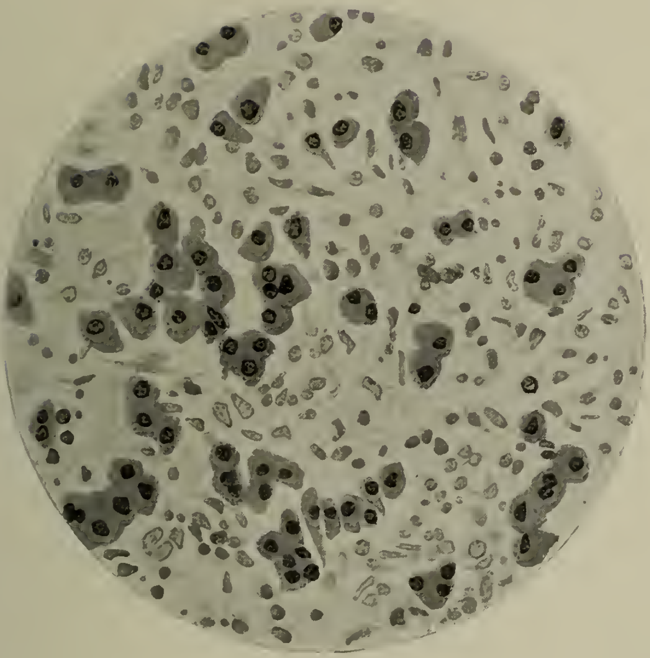
Giant cells from the margin of a young gumma of the skin. Four or five large multinucleate syncytia are seen in the figure, with plasma cells, fibroblasts, and endothelium. The specimen was stained with polychrome methylene blue. × 500.

From a preparation by Mr. J. E. R. McDonagh.



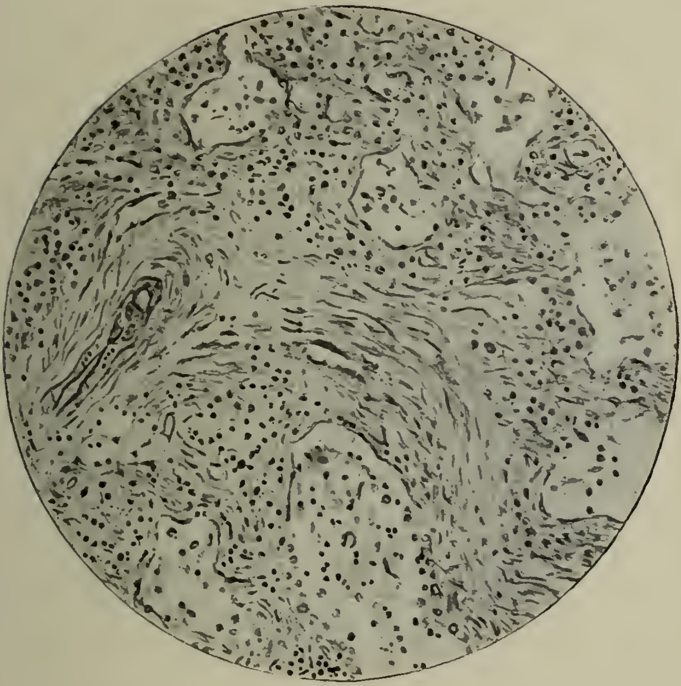
Syphilitic cirrhosis of the liver. Apart from the grosser fibrous bands, the lower cells are separated from one another by fine strands of newly-formed connective tissue. Various stages of atrophy are seen in the liver cells. × 150.

PLATE XXXI



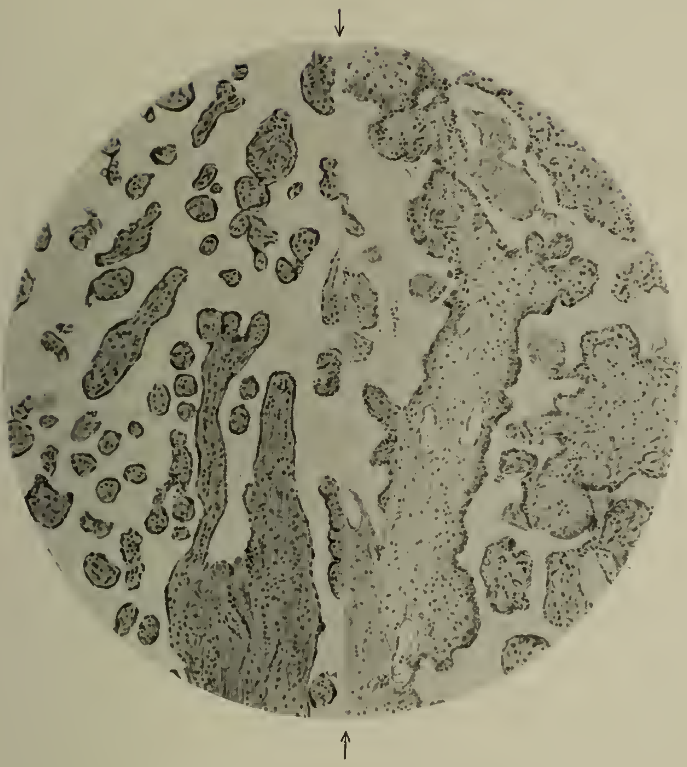
Section through the liver of a syphilitic infant which did not long survive birth. No gummata were present in the liver, but a uniform pericellular cirrhosis was everywhere found. The changes seen in the figure are characteristic, but somewhat extreme. The liver cells are separated into small groups of two and three by an abundant development of young and very cellular fibrous tissue. × 400.

PLATE XXXII



Syphilitic pneumonia. Section through the lung of a still-born syphilitic infant. The lung was airless and in the condition known as 'white hepatization'. The alveolar walls are greatly thickened by young fibrous tissue, while the cavities of the alveoli are occupied by cast-off epithelium, with a few leucocytes. A broad band of fibrous tissue crosses the section; the artery, which is seen in longitudinal section, shows this to be a perivascular fibrosis. × 200.

Plate XXXIII



Showing the contrast between a syphilitic and a normal placenta. The left-hand half of the figure is drawn from a normal placenta at term. The right-hand half is drawn to the same scale from a section of the enlarged and heavy placenta of a syphilitic pregnancy which went on to term. The villi of the affected placenta are seen to be greatly thickened, chiefly by a mucoid transformation of their ground substance. × 100.

From preparations kindly lent by Dr. H. Williamson.

THE PRIMARY LESION AND EARLY SECONDARY SYMPTOMS OF SYPHILIS AS SEEN IN THE MALE

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CHAPTER XVI

THE PRIMARY GENITAL LESION AND EXTRA-GENITAL CHANCRES, AS SEEN IN THE MALE

The question of the antiquity of syphilis, together with its history, have formed the subjects of innumerable essays; it must suffice here to inquire as to the earliest mention which is made with reference to the primary lesion of the disease.

In the history of the early ravages of syphilis very accurate accounts are given of its appearance and progress.

Marcellus Cumanus, writing in 1495, observes 'that he had seen many officers and foot-soldiers while he was in the camp at Navarre to have several scabs and pustules breaking out in the face and spreading all over the rest of their bodies, the first of which appeared usually under the prepuce or on the outside like a grain of millet, sometimes behind the glans with slight itch; at other times a single pustule would arise like a little bladder, without pain, but itching also: if rubbed or scratched there arose an ulcer erosive and smarting like the sting of an ant'.

John of Vigo [1460–1520?], writing of the disease at Genoa, says: 'Eius origo in partibus genitalibus, viz. in vulva in mulieribus, et in virga in hominibus semper fere fuit cum pustulis parvis interdum lividi coloris, aliquando nigri; nonnunquam subalbidi; cum callositate eas circumdante.'

These descriptions appear to me to be deserving of particular attention, showing, as they do, an accurate knowledge and affording proof that the hardened and callous base of the ulceration, which was assumed by Hunter many years after as the peculiar and distinctive character of chancre, did not escape the notice of the very earliest writers on this disease.

John Hunter, indeed, writing on the same malady, assures us ‘that mercurial ointment rubbed twice a day on the legs and arms till the gums began to swell and the teeth to loosen was the best and most efficacious remedy for the curing this disorder’.

The first lesion in acquired syphilis is a chancre; this is followed by general glandular enlargement, by eruptions of the skin, usually symmetrical, superficial, and associated with very similar affections of the mucous membranes; at a later stage by chronic inflammation and infiltration of the cellulo-vascular tissues, the bones, and the periosteum, and finally by the formation of small inflammatory swellings called gummata, which may appear in any portion of the body, but which generally develop in the connective tissues.

Stages of Syphilis. In accordance with the clinical course, the phenomena of syphilis are classed under certain stages or periods.

1. The Stage of Primary Incubation is the interval between exposure to infection and the appearance of the chancre.
2. The Stage of Primary Symptoms is the period during which the chancre develops and the adjacent glands become enlarged.
3. The Stage of Secondary Incubation is the time elapsing between the appearance of the chancre and the development of secondary symptoms.
4. The Stage of Secondary Symptoms: during this stage fever, neuralgic pains, anaemia, syphilides of the skin and mucous membranes, make their appearance.
5. The Intermediate Stage: during this time the patient may be entirely free from all signs and symptoms of the disease, or may suffer from some of the slighter and more irregular symptoms.
6. The Tertiary Stage: this is characterized by the formation of gummata, chronic periostitis and osteitis, ulcerations closely resembling those caused by tubercle, diseases of the nervous system, &c.

In the above classification of syphilis it may be mentioned that the first four stages are generally more or less definitely marked; the fifth and sixth are, on the other hand, not so marked.

The Stage of Primary Incubation. After exposure to contagion the lesion of syphilis does not show itself at once, and although there might appear to be little reason to suppose that the virus of syphilis remains entirely localised during the time between inoculation and the appearance of the chancre, evidence has been accumulating during recent years, which points to this being the case—at least up to a certain time. Metchnikoff [vol. ii] showed, some time ago, that the application of a mercurial ointment in and around the immediate point of inoculation apparently destroys the virus of the disease, so that after the application no constitutional symptoms of syphilis follow. It can be easily demonstrated that, in a chancre which contains many spirochaetes, the application of a mercurial ointment causes immediate disappearance of these organisms.

Again, the excision of an undoubted induration, which is quite different from the excision of a chancre, has sometimes prevented the occurrence of constitutional or other syphilitic symptoms, and when this excision has failed it is probable that it was not carried out thoroughly.

As to the length of time during which the syphilitic virus remains more or less localised it is hard to say, for whilst Metchnikoff limits it to a couple of hours, others put it at a much longer period. One fact is suggestive, that a chancre is auto-inoculable up to ten days after its appearance, and then ceases to be capable of inoculation, a fact which suggests that the time necessary for general infection of the system is much longer than has been previously supposed.

During this stage, then, there are no general or local symptoms. As to the length of the primary incubation stage—it may be as short as ten days and as long as three months, but this is exceptional. Experiments both in the human subject and in monkeys show that the average incubation period is twenty-five to thirty days; taking this fact with our own practical and accumulated experience, one will be justified in putting down three weeks to one month as the average time of this period.

As a rule it may be suspected that a chancre which appears more than ten days after exposure to contagion is probably syphilitic.

The Stage of Primary Symptoms. After the period of inoculation, the primary lesion of syphilis, a chancre, appears.

The chancre always appears at the point of inoculation. It begins as an erythematous spot, shortly after it becomes a superficial papule, and this generally becomes eroded. This latter condition is accidental; for, if protected, erosion does not take place, yet ulceration may follow; this is usually caused by secondary infection.

When first seen, a chancre generally presents itself as a superficial erosion. This gradually extends in circumference and depth, and in the course of a few days is surrounded by a well-marked area of induration. In shape the erosion is circular and of a deep red colour, changing to grey later, and exuding a thin sanious fluid.

When actual ulceration exists, a cup-shaped depression with sloping sides is formed, in the centre of this is a false membrane which, when stripped off, causes oozing of dark-red blood from the surface. Frequently the chancre appears as a simple abrasion.

The primary lesion causes but little local, and no constitutional, disturbance of any kind; the first indication which draws the patient's attention to it is generally an itching at the site.

Histology of the Chancre. A chancre is formed by a small-celled infiltration and hyperplasia of the connective-tissue cells. There is an inflammation of the internal coat of the small arterioles and veins. This mass of cell-infiltration is supported in a mesh-work of thickened blood-vessels; some of these latter are entirely obliterated by sclerosis. It is this condition which constitutes the specific induration, and the amount of induration will depend on the depth of the vessels which are affected.

INDURATION. For the first five or six days there is nothing very characteristic about the chancre, but at the end of this time the induration becomes perceptible, and it continues to increase until it reaches its maximum in about two weeks from the first appearance of the chancre.

Induration is sometimes entirely absent, but it is present in the great majority of cases. The form that induration assumes varies, and it is generally spoken of from the sensation it conveys to the fingers on palpation.

Forms of Induration. Indurations assume different shapes and forms, and accordingly these may be termed :—

1. *Laminated Induration.* Here the hardening round the chancre is so thin that if taken between the fingers it feels as if a disk of paper had been inserted in the superficial layers of the skin.

2. *Parchment Induration.* When the sensation conveyed is as if the lesion was placed on a piece of parchment.

3. *Nodular Induration.* In this case the induration is dense and hard, like a nodule of cartilage. This is the most characteristic form.

4. *Annular Induration.* The hardness in this instance, as its name suggests, forms a dense ring round the sore.

Modes of detecting Induration. Induration is best made out by pinching between the thumb and index finger the parts surrounding the chancre, when, if present, the hardness will be felt. Induration will vary as to amount, character, &c., according to the site upon which it happens to be placed. Thus, when situated on the glans penis or mucous membrane of the prepuce, it is generally well marked, much more so than when placed on the skin of the penis or anywhere else on the general integument of the body.

Induration is not the result of Inflammation. Induration of a chancre is a peculiar hardness of the tissues around and beneath the sore. Simple inflammation may occasion an effusion of plastic lymph about a sore, but specific induration is formed without any having occurred. It is formed, as the French say, 'à froid.' The deposit takes place without pain, heat, redness, or swelling. Any hardening due to inflammatory action is neither defined nor circumscribed. It feels as if it shades off into the adjacent tissues. On the contrary, that due to specific action is circumscribed, more or less defined, and the sensation conveyed to the fingers is quite different, being firm, hard, and resistant, like a split pea. Induration usually remains after the surface of the chancre has healed, but it generally disappears in about six weeks, though it may persist for months and even years.

Recurring or Relapsing Induration. 'Redux chancre.' The relapsing chancre has generally been described as a fresh induration appearing at, or perhaps near, the site of an old chancre. This induration may make its appearance without any apparent cause at any time from a few weeks after the healing of the sore up to ten or twelve years afterwards. As a rule the surface of this induration remains intact, but it often becomes eroded and ulcerated, and may then simulate a disintegrating gumma. John Hunter, in his 'Treatise on the Venereal Disease' (part iv, chap. iii, § 7), says: 'In the cure of chancres I have sometimes seen, when the original chancre has been doing well and probably nearly cured, that new ones have broken out upon the prepuce near to the first, and have put on all the appearance of a chancre; but such I have always treated as not venereal.' And again in the same work (chap. v, § 2): 'It often happens that after chancres are healed, and all the virus gone, the cicatrices ulcerate again and break out in the form of chancres' ... 'As they are not venereal their treatment becomes difficult, for the cure consists more in preventing a return than in the healing up of the present sores.'

It is hard to conceive why Hunter should consider these recurring chancres to be non-venereal, and express himself so definitely in the matter.

The True Relapsing Chancre. Sometimes, having entirely disappeared under treatment, the induration reappears on the original site of the chancre and assumes exactly its previous condition as regards appearance, feel, and extent.

As a rule its surface is unbroken, but it may become eroded, and in many cases the chancre resumes its former condition. To my mind such chancres are closely connected with the nature of the treatment adopted, as I have observed that the return of the induration nearly always coincides with the temporary or total suspension of mercury. One case in particular I recall to mind, in which a large induration, having disappeared under a course of mercurial rubbing at Aachen, reappeared in its original shape a month after the mercurial course had finished, and this sequence of events happened in the same chancre on three separate occasions. The induration was made to disappear under more prolonged mercurial treatment.

This has been my experience, more or less, with all the other cases in which I have observed the true relapsing chancre.

Situation of Chancres. The primary lesion of syphilis may be found on any part of the body. Those situated in the genital or peri-genital regions are called genital chancres, whilst those occurring in any other part of the body are termed extra-genital.

Genital Chancres. At least two-thirds of all chancres occurring in the male are found on the mucous membrane of the prepuce, in or just behind the corona, or on the surface of the glans penis. Sometimes they are found at the urinary meatus just within the orifice of the urethra, the base of the penis, the scrotum, groin, and anus. The following table shows the seat of 481 chancres in men observed in the Hôpital du Midi during a certain period :—

Chancres on glans and prepuce	314
„ on skin of penis	60
„ on various parts of penis	11
„ on urinary meatus	32
„ within the urethra	6
„ on scrotum and pre-scrotal angle	17
„ of anus	11
„ of lips	6
„ of tongue	12
„ of nose	8
„ of eyelid	1
„ of finger	2
„ of leg	1
	481

Varieties of Genital Chancres. The chancre is generally single, but may be multiple either if it is genital or extragenital. Although it may appear in a great many varieties, the majority present certain well-marked characteristics, viz :—

1. Chancrous erosion.
2. „ ulceration.
3. „ indurated papule.

The first is the most frequent and forms about a fourth of all genital chancres. When first seen it looks like a small abrasion. This slowly enlarges and assumes an oval shape surrounded by a dusky areola. The surface is raw and polished. Soon it becomes covered by a grey false membrane and exudes a blood-stained serum. Induration develops in about a week.

Pain and Inflammation. Absence of pain and inflammation is common to all uncomplicated chancres, the patient's attention being generally first drawn to the lesion by some degree of itching; but even this may be absent and the chancre may attain full development before it is discovered: this is more likely to be the case when there is induration without any breach of surface.

Chancrous Ulceration. This differs from the first-named chancre in that whereas erosion is simply desquamation of the epithelium, in ulceration the true skin is involved.

An ulcerating chancre may be either superficial or deep. In the former the true skin is partially, but not completely, destroyed. The resulting ulcer is fairly deep with slanting edges. Its surface is usually covered by a grey false membrane and the exudation is thin, scanty, and sanious. In these chancres induration is usually well-marked, and may be found in any of the forms already quoted, though it is more usually the nodular or cartilaginous.

The Deeply Ulcerated Chancre. This is fairly frequent. Ulceration destroys the whole of the true skin, eating into the tissues beneath it. A deep ulcer with more or less vertical or even excavated edges results. It is surrounded by hard cartilaginous edges which in some cases form a thin ring round the chancre. In these chancres the whole of the pre-existing indurated mass may be eaten away, and no induration can be found; this will obviously render diagnosis difficult.

The Indurated Papule. This chancre begins and ends in a hard, raised, dusky-red elevation. The surface remains intact, and, as a rule, dry, but is sometimes covered by dried, scaly epithelium. As to size, it may be an inch in diameter or even larger, though it is sometimes no bigger than a quarter of an inch across.

Considering its size and that from beginning to end the lesion may not give the least trouble it can be easily conceived how readily it may pass undetected.

Although chancres generally assume the character of one of the above varieties they sometimes present erratic forms.

1. *Herpetic Chancre.* This, although resembling herpes, differs from it in being single, not exuding the characteristic discharge of herpes, having a hard base and a different clinical history.

2. *The 'Silvery Spot'*, first described by Martin, of New York, is a not uncommon sore, and of this I have seen many examples. It appears usually on the glans penis, and when first seen looks just like the mark left after the application of a stick of silver nitrate, the surface of this gradually darkens and eventually becomes dark yellow, at the same time its base and sides become indurated.

3. *The Mixed Chancre.* A lesion which results from the double action of chancroidal and syphilitic virus. The character of the chancre will depend on which of the poisons was first inoculated. In the case of simultaneous double inoculation, the chancroid appears first, and may almost have run its course before induration shows itself, but more usually the soft chancre persists, and round this eventually induration appears.

As previously remarked, the general character of a chancre will be influenced a great deal by its situation.

Chancre on the Surface of the Glans Penis. This is at first flat, but soon becomes depressed and surrounded by a well-marked indurated edge. When taken between the fingers, induration of the laminated variety is felt.

Chancre of the Corona or Preputial Sulcus. (Plate XXXIV.) This usually has a tendency to be raised, induration is well-marked, extensive, and often is nodular in character.

Chancre of the Urinary Meatus. In these chancres either one or both lips of the meatus may be involved, but both are generally affected. The mucous membrane is found thickened and the lips are glued together by a scanty and viscid discharge. Induration in these chancres, although limited, is always well marked.

Needless to say,—chancres of the meatus may be mistaken for gonorrhoeal ulceration, and vice versa, and further, that a correct diagnosis is rendered all the more difficult when gonorrhoea co-exists.

Chancres of the Urethra. I believe these to be more common than is generally supposed ; the reason for this is obvious. They are concealed from view, cause little disturbance, and are extremely likely to be mistaken for gonorrhoea, indeed in nine out of ten cases a diagnosis of gonorrhoea is made, at least until further symptoms are well developed. Chancres attacking the urethra are usually met with just within the meatus or in the fossa navicularis, but may occur lower down the urethra. There is pain on micturition, a slight thin and yellow discharge ; hardness can be detected along the urethra in a circumscribed degree, and sometimes when the finger is passed along the course of the canal, it gives the sensation as if there was 'a piece of the stem of a clay pipe' embedded there. These lesions can best be detected by internal manipulation, by means of an olive-headed bougie, or they may be seen by the urethroscope.

Chancre at the Base of the Penis (Plate XXXVI) occurs on the skin in or about the base of the penis. When first seen it looks like a scratch or abrasion about the size of a pea. This enlarges slowly, becomes eroded, flat or depressed, until it is half an inch or even an inch in diameter in some cases. It is nearly always circular in shape, its edges are markedly hard, and when taken between the fingers laminated induration is well marked, in fact it is in these chancres that this form of induration is best marked.

The surface of the chancre erodes and sometimes ulcerates, but the latter is rare. It is covered with a whitish-yellow false membrane, on the removal of which a weeping surface is left. The surface sometimes looks like the top of a pepper castor.

Chancre of the Scrotum. Commencces as a circumscribed erythema. The skin soon desquamates and leaves little cracks or fissures exuding a clear serum ; these cracks unite by erosion, and a shallow ulcer, circular in shape, situated on a hard base with well-marked indurated edges, remains.

In other cases the surface of this form of chancre is covered with brownish crusts of dried epithelium which keep on re-forming as often as they are removed ; again, the primary syphilitic lesion in this locality may closely resemble the form of a tubercle.

Preputial Chancres. (Plate XXXVIII.) When placed at the end or termination of the prepuce these chancres are ragged, and give the end of the prepuce the appearance of having been split in one or two directions. These splits look, at first, like scratches, the edges of which are indurated and generally inflamed. The prepuce in this situation is usually thickened.

Sub-Preputial (*or concealed*) *Chancres.* A chancre of the prepuce may be rendered invisible owing to phimosis either congenital or acquired, the latter being the result of the inflammation caused by the chancre itself.

In this case, in addition to the phimosis, there will be a thin yellowish discharge which can be gently squeezed out, little or no pain on micturition, and no other sign of gonorrhoea. Should an indurated sore be present beneath the foreskin, this hardening can generally be felt by manipulating the part with the fingers. But in any case the surgeon should seldom be long in doubt, as means ought to be taken to expose the sore at once.

Chancres of the Anus may be situated at the margin of, or entirely within, the anus. The former generally present a thickened, fissured, and ulcerated surface, devoid of deep redness. They are of a rose-red tint, the base, although indurated, is not decidedly so. Sometimes these chancres assume the character of fissures ; the margins are pale and smooth, the surface pale red. Their bases are resistant to the touch, and are far less tender than ordinary ‘ fissures ’ of the anus—an important point in diagnosis.

When situated within the anus the chancre will, of course, be concealed and will require examination with a speculum. The chancre looks like a deep erosion or ulceration with a more or less smooth surface. Induration of its base may exist, but it is difficult to make this out here.

Chancre of the Groin. This chancre comes within the class of peri-genital chancres. It may occur from direct inoculation, or as a secondary infection of an open bubo. In the first case it will appear like the indurated chancre of the general integument which will be afterwards described. Should an open bubo become infected with syphilitic virus, the chancre will generally attack one or both lips of the wound. The latter remains gaping, and a sore or nodule appears on one of the lips. This slowly enlarges until an ulcer is formed which soon becomes planted on a well-marked indurated base. The open bubo may continue to heal all over except the part at and about the chancre, which remains open and indolent looking. (Plate XXXIX.)

Complications of Chancre. The appearance and progress of all chancres may be modified by certain events :—(1) simple or septic inflammation, (2) chancroid inflammation, (3) phagedaena.

Simple or Septic Inflammation may attack any chancre, the former being generally brought on by the employment of caustics and other strong applications; the latter by pyogenic micro-organisms. Under these circumstances the chancre becomes red, painful, and a neighbouring gland may inflame and suppurate. This inflammation will necessarily change the appearance of the chancre, at any rate for the time being.

Chancroid Inflammation. The chancroid virus may be implanted at the same time as the syphilitic, or subsequently the latter may become inoculated with the former. In either case the character of the syphilitic chancre will be modified in appearance. Of course it would be quite possible for the chancroid to heal up before the syphilitic virus took effect, but this would be the exception ; more commonly the chancroid persists, the spreading, inflamed, punched-out-looking ulcer becoming gradually enveloped in induration as the full local development of the syphilitic lesion is reached. In the other case, where the chancroid virus is inoculated on the true chancre, the result is chancroidal ulceration, on the disappearance of which the induration remains. Ulceration of a chancroid may cause sloughing of an indurated mass, with the result that no local indication of syphilis may be found. (Plate XXXVII.)

A sore of the above description is called a ‘ mixed chancre ’.

Phagedaena. Inflammation of a chancre may be the cause of phagedaena : the engorgement of the tissues may be so great as to cause loss of vitality with resulting gangrene, or cause more chronic ulceration of a serpigenous character. (Plate XXXIX.)

Certain factors influence the onset of phagedaena, and some individuals are more predisposed to it than others. Any lowering of the system leads up to it, the cause of this being generally starvation, malaise, or alcoholism, it is more likely to follow inoculation from an individual of a different race than otherwise.

In the 'Medico-Chirurgical Transactions', 1813, is an article by William Fergusson (1772–1846), Inspector-General of Hospitals to the Portuguese Army—'Observations on the Venereal Disease in Portugal'. Writing of phagedaena, he says ('Medico-Chir. Trans.,' vol. iv, p. 10):—

'It is certain that all changes of climate from a cold to a warmer temperature predispose the human frame to febrile affections or other forms of acute disease: and that the English, from their mode of life, always incautious and frequently intemperate, are exposed in a particular manner to suffer from this predisposition. And if, previous to this attack, with their constitutions on the point of exploding into the acute forms of fever or dysentery, they should have the misfortune to be affected with venereal ulceration, the elements of the disease which had previously been prepared within their bodies, and would have manifested themselves in a general constitutional affection, at a given period, according to their own laws, are diverted by this casualty into new channels, and make their exit as a local form of fever in the shape of *phagedaenic ulceration.*

'To make this understood, I shall endeavour to illustrate it by a short case. Shortly after the battle of Vimiera, while making an inspection of the cantonments near Lisbon, I was called to by an officer, a friend of mine, who earnestly implored my assistance. I found him, four days after a connexion in Lisbon, with the whole penis enormously swelled, of a deep-red colour; malignant and ugly chancres on different parts of the prepuce, and two on the glans penis, the appearance of which I can compare to nothing but the holes made by a rusty nail in a piece of mahogany or logwood. He was young, robust, and plethoric, and of the sanguine temperament. The skin was hot, pulse sharp and quick, tongue white, and eyes red, though he had been guilty of no intemperance in drinking. The catastrophe, if left to nature, ere mercury was in fact at hand, or a few doses of bark, wine and opium, would have inevitably sealed his fate; but I caused him to be copiously blooded, applied the coldest acetous lotion to the part, purged him most freely with neutral salts, and enjoined every part of the anti-phlogistic regimen.

'The success was perfect, the tumification speedily subsided; in a few days all the sores were in a state of the healthiest suppuration, and I have no doubt, so thoroughly had the specific contagion been superseded by the violence of the inflammation, would have healed safely without mercury, had either the patient's fears or my own responsibility permitted me to run the risk.

'The woman who communicated the infection was an opera dancer in Lisbon, apparently in perfect health, who continued upon the stage for many months afterwards, occasionally infecting others, without anything extraordinary, as far as I could learn, in the nature of the symptoms.'

Phagedaena may attack a chancre at any time, either at the beginning or later on, and I have seen it attack a very late relapsing chancre.

As a rule phagedaenic ulceration does not extend beyond the limits of the induration, which it generally destroys entirely. It may cause profuse haemorrhage, perforation, and stricture of the urethra.

Phagedaena is certainly sometimes infectious, or contagious, in that it produces a like sore on inoculation. On the other hand, I have known a case where one patient contracted a phagedaenic sore from a woman; while others who had connexion from the same source only developed a simple indurated papule.

Diagnosis of Chancre. Although perhaps under ordinary conditions the diagnosis of chancre is comparatively easy, it must be remembered that there is no certain sign, and although one may have formed a strong opinion as to the nature of a sore, still it is a safe plan to give no positive opinion from the examination of the lesion itself. Should a sore be seen with a history of having appeared within five days after exposure, and that it has been painful since its commencement, when observed the sore is exuding pus, and no glands are indolently enlarged although some are inflamed; on treatment no induration develops at site of this sore within ten days, and the ulceration proves amenable to local treatment—the probability is that such a sore is non-syphilitic in nature.

On the other hand, should a sore which has appeared five days after exposure to infection and has become indurated later on, suddenly become inflamed, and sloughing takes place which destroys all the induration, so that at a later date the lesion comes to have the appearance and character of a simple sore, the probability is that it is a 'mixed chancre'. This opinion will be strengthened by finding multiple, indolent, glandular enlargements in the neighbourhood even though there be a suppurating bubo.

The Syphilitic Chancre. (1) *Incubation.* A sore beginning in from ten days to four weeks after exposure.

(2) When it begins in a painless macule or slight excoriation, which persists in spite of all local treatment: when it slowly spreads without inflammation: when it becomes distinctly indurated and the induration is circumscribed: when it exudes a thin scanty discharge, or its surface is covered with crusts or false membrane. The chances are that such a sore is a chancre.

(3) Should the neighbouring glands increase in size without pain or inflammation, forming a chain of little tumours, the evidence of the syphilitic nature of the lesion is very much strengthened.

(4) The discovery by Schaudinn of the *Spirochaete pallida* as the pathogenic microbe of syphilis is a distinct gain to the clinical observer of chancres. This organism can generally be demonstrated in the true chancre. (For methods of examination see pp. 86 to 94.)

The difficulties of diagnosis are greatest at the beginning, and the nature of the case becomes more manifest the older it becomes. The main difficulties met with are (1) that the history of incubation is, to say the least, often vague and uncertain, (2) induration may be altogether absent, or marked, or so slight as to be indefinable.

Undoubtedly cases of syphilitic sores have been observed where there was entire absence of induration; on the other hand the induration may have been most difficult to define owing to the infiltration caused by inflammation, or where it has been destroyed by subsequent ulceration.

The enlargement of neighbouring glands may be absent (under exceptional circumstances), but, on the other hand, it must be remembered that many perfectly healthy patients have hard and movable glands in both groins. Hence the great necessity of repeatedly examining suspected cases to determine whether the enlargement is progressive or not.

Differential Diagnosis of Genital Chancres. The diagnosis as well as the characters of mixed chancre have already been discussed, suffice it to say again that in the case of a sore appearing later than ten days after exposure which is followed by induration, which becomes inflamed and ulcerated with consequent destruction of the induration and then presents only the features of a simple sore, the probability is that it is a mixed chancre. This surmise will be further strengthened if the lymphatic glands in the neighbourhood become indolently enlarged.

DIAGNOSTIC POINTS BETWEEN A CHANCRE AND A CHANCROID.

	Chancre.	*Chancroid.*
Origin.	Due to infection from syphilitic lesion, blood, or other syphilitic discharge.	Due to inoculation from chancroidal discharge.
Incubation.	Over ten days: average time, three to four weeks.	No definite period: generally under five days.
Commencement.	Erosion, papule, or ulcer.	Pustule, or open ulcer.
Number.	Single: at times multiple (exceptional).	As a rule multiple: often on opposing surfaces from auto-inoculation.
Shape.	Symmetrically irregular.	Round, oval.
Depth.	Superficial erosion, scooped-out, flat, or elevated.	Deep, perforating whole thickness of skin and mucous membrane.
Edges.	Sloping.	Abrupt and sharply cut.
Floor.	Red, livid, copper-coloured: often iridescent. Sometimes covered with false membrane.	Whitish, grey, or yellow.
Secretion.	Scanty, sanious serum. Not readily auto-inoculable, and only so during first ten days of existence.	Abundant and purulent: readily inoculable.

<table>
<tr><th><i>Chancre.</i></th><th><i>Chancroid.</i></th></tr>
<tr><td colspan="2"><i>Induration.</i></td></tr>
<tr><td>The rule: firm, cartilaginous, circumscribed.</td><td>No induration as a rule: if present not circumscribed, but shades off into adjacent tissues.</td></tr>
<tr><td colspan="2"><i>Frequency in one subject.</i></td></tr>
<tr><td>One chancre affords protection in ninety-nine out of one hundred cases.</td><td>Affords no protection.</td></tr>
<tr><td colspan="2"><i>Glandular enlargement.</i></td></tr>
<tr><td>Neighbouring glands indolently enlarged; firm, movable, no inflammation. When sore is situated on penis, glands of both groins uniformly enlarged.</td><td>Inflamed, painful, irregular suppuration. Glands on both sides not uniformly enlarged.</td></tr>
<tr><td colspan="2"><i>Micro-organisms.</i></td></tr>
<tr><td><i>Spirochaete pallida</i> generally found.</td><td><i>Spirochaete pallida</i> never present.</td></tr>
<tr><td colspan="2"><i>Effect of treatment.</i></td></tr>
<tr><td>Local treatment ineffectual.</td><td>Local treatment curative.</td></tr>
</table>

Should phimosis be present so that the glans or sub-prepuce cannot be seen, diagnosis is always difficult. In such cases the following points will have to be considered:—

<table>
<tr><th>SYPHILITIC SUB-PREPUTIAL CHANCRE.</th><th>SUB-PREPUTIAL NON-SYPHILITIC ULCERATION.</th></tr>
<tr><td colspan="2"><i>Incubation.</i></td></tr>
<tr><td>Never, or seldom, less than ten days: usually three weeks or a month.</td><td>None: always less than ten days.</td></tr>
<tr><td colspan="2"><i>Inflammatory signs.</i></td></tr>
<tr><td>Not marked.</td><td>Well marked.</td></tr>
<tr><td colspan="2"><i>Swelling.</i></td></tr>
<tr><td>Hard, circumscribed.</td><td>Diffuse and oedematous: cannot be isolated.</td></tr>
<tr><td colspan="2"><i>Discharge.</i></td></tr>
<tr><td>Scanty, thin, and sanious: not readily auto-inoculable.</td><td>Profuse, purulent, thick: readily auto-inoculable.</td></tr>
<tr><td colspan="2"><i>Buboes.</i></td></tr>
<tr><td>Bilateral, indolent, uniformly enlarged.</td><td>Single, inflammatory, suppurating.</td></tr>
<tr><td colspan="2"><i>Micro-organisms (specific).</i></td></tr>
<tr><td><i>Spirochaete pallida</i> may be found.</td><td><i>Spirochaete pallida</i> never found.</td></tr>
</table>

Auto-Inoculation. It was generally believed until recently that the chancre was never auto-inoculable, but it is now a well-established fact that this is not entirely the case, and that during at least the first ten days of the chancre's existence it is auto-inoculable, that is, capable of reproducing a lesion similar to itself if inoculated in some other part of the body: at no time is it readily so, and never to the same extent as a chancroid.

Queyrat has reported cases of auto-inoculation of chancres, and at the Annual Meeting of the British Medical Association held at Toronto in August, 1906, several cases were cited. Personally, at the Military Hospital, Rochester Row, London, I have succeeded on several occasions in producing a second lesion identical in every respect, by inoculating a patient on some other part of the body from a typical chancre situated on the penis during the first ten days of its existence. All the cases so inoculated proved by later constitutional symptoms to be syphilitic. After ten days I found it impossible to reproduce an identical sore, or anything like it; as a rule a small inflammatory pustule was the only result.

From later experiments made by myself, I find that mercurialization of the patient renders auto-inoculation almost impossible, even during the first ten days.

The Specific Organism of Chancre. It need hardly be said that the discovery by Schaudinn, in 1905, of the *Spirochaete pallida* as the assumed organism of syphilis, a fact which is now recognized, is of the greatest importance concerning all stages of the disease. Although I have no intention of entering at all fully into this great discovery as regards its bearings on syphilis generally, it will be necessary to consider it in connexion with the primary lesion.

The *Spirochaete pallida* is constantly found in the exudation from the punctured surface of a non-eroded indurated papule, in sections of the papule, or in scrapings from an ordinary eroded chancre, whilst it has never been seen in non-syphilitic dermatitis, i.e. soft chancre, herpes, or balanitis. However, a word of warning is necessary as regards the presence or absence of the *Spirochaete pallida* in a sore: although it is found much more often than not in a chancre, still it sometimes cannot be discovered, this is partly explained by the difficulty of technique, so that a negative examination does not prove that the lesion is non-syphilitic; on the other hand its presence is conclusive of the syphilitic nature of the lesion. Thus the discovery made by Schaudinn is most valuable from a diagnostic point of view as regards the primary lesions of syphilis.

An examination for the spirochaete may be conducted by lightly scarifying the surface of an unbroken syphilitic, or presumedly syphilitic, induration, and taking a smear therefrom or from the scrapings or exudations of an eroded chancre. Blood and pus should be avoided, and it may be necessary to examine half a dozen specimens before one succeeds in finding the microbe. An excellent method is to apply a vesicant in the immediate proximity of the sore and to examine the liquid taken from the vesicle thus formed from spirochaetes. For fuller details see pp. 86–94. Research has shown that the *Spirochaete pallida* is rarely found in the blood, but is generally present in the walls of the blood-vessels themselves and around them, showing that the organism is conveyed by the blood, but that the latter is not the medium in which it develops.

Effect of Mercury on the Spirochaete pallida. The organism disappears rapidly under the influence of mercury. The writer noticed very soon after its discovery, that in cases where previous to the administration of mercury they had been easily detected, they became difficult to find the second day after an intramuscular injection of one grain of metallic mercury, and that it was impossible to demonstrate them within two days after a second injection. Further, that even the local application of black wash to a chancre rendered their detection very difficult. This latter fact had already been noticed by Metchnikoff and Roux (see vol. ii), as regards the effect of the local application of mercury at the point of inoculation.

Their experiments on chimpanzees and monkeys showed that inunction with mercurial ointment at the point of inoculation an hour or an hour and a half after the introduction of the virus prevented development of the disease. They afterwards performed the same experiment in a human being with entire success. Hence their suggestion of the application of calomel ointment as soon after exposure as possible, as a preventive treatment.

Neisser does not confirm the above favourable results. But in spite of this and seeing, as we can daily, the marvellous effect of even weak solutions of mercury in causing the disappearance of the spirochaete when locally applied, and this some hours after inoculation, the author cannot help thinking that there is much in the suggestion of Metchnikoff and Roux.

Is the Spirochaete pallida found in any other Disease? Curiously enough the one other disease in which this organism is said to have been found is that which has been regarded by some as a form of syphilis; this is yaws (parangi or pian). In this disease Castellani has found a spirochaete which Schaudinn himself stated closely resembled the *Spirochaete pallida.* Whether the two diseases are one and the same is still open to discussion; but it must suffice to consider here the primary lesion of both. In syphilis there is nearly invariably a well-marked primary lesion in the shape of the chancre; be it a papule, an erosion, or ulcer, induration eventually develops at the site of the sore, accompanied by a bilateral inflammation of the neighbouring glands. The glands are hard, movable, and indolent. The chancre, although auto-inoculable during the first ten days, is not so at a later period.

In yaws, the existence of a primary lesion is questionable. Some of the most careful observers deny that there is any; on the other hand Nuna Rab declares there is, and describes it as a papule with pale yellow material at its apex, the lesion may remain papular or may ulcerate. Most authorities agree that what might be called the first lesion in yaws is of the same nature as the numerous secondary lesions, and that typical induration is never developed. In yaws every lesion, primary as well as secondary, is always auto-inoculable and that at all times. The indolent glandular enlargements are absent in yaws, and if there is any enlargement it is of an inflammatory nature.

No Primary Lesion in 'Yaws'. The weight of evidence goes to prove that in this disease, be it a form of syphilis or not, there is no typical primary lesion which will coincide with the chancre of syphilis. On the other hand it is quite possible that a 'yaw' located in some situations, may be taken for a chancre—take, for instance, one occurring under a toenail (onychia).

Neisser and Bauermann have succeeded in inoculating apes with yaws. The infection can be transmitted from ape to ape, and those infected with syphilis are still susceptible to yaws.

EXTRA-GENITAL CHANCRES

may be situated on any part of the body, but are more often found on the mouth, tongue, and lips, than any other part. The difficulty of diagnosing an extra-genital chancre may arise from its position or locality. They are as a rule single.

The usual seats of extra-genital chancres are the lips, tongue, mucous surface of the mouth and pharynx, fingers, and face.

Modes of Conveyance. Syphilis may be conveyed to the neighbourhood of the mouth (1) by direct infection from a syphilitic lesion, or by kissing; (2) by intermediate contagion through the agency of contaminated spoons, forks, drinking utensils, pipes, penholders, &c., &c., or again through infected surgical appliances such as spatulas or by dental instruments.

Chancre of the Lip. (Plate LII.) This begins generally as a chap, fissure, erosion, or ulcer. It is usually situated a little outside the median line. To begin with there is nothing characteristic about it; but as days go on it slowly extends, is indolent, and soon becomes markedly indurated. Induration is always well marked in these chancres. In the course of a couple of weeks the submental glands become indolently and painlessly enlarged.

In these cases the whole lip soon becomes very much congested, and when taken between the fingers feels like a lump of gristle surrounded by some fatty substance. My own experience is that the upper lip is more often the site of the lesion, probably from its being more prominent than the lower.

Its appearance is that of an indolent, elevated sore, pustule or papule, with circumscribed indurated edges. The surface, if broken, is smooth, and exudes a scanty, glistening discharge. It is, as a rule, quite painless unless the lip becomes inflamed.

Labial chancres may be mistaken for labial epithelioma (see Plate LII).

The following points may serve to differentiate them :—

	Labial chancre.	*Labial epithelioma.*
Age.	Any age.	Occurs almost always after middle age.
Sex.	Both sexes indifferently.	Nearly always affects males.
Seat.	Both, but more often the *upper* lip.	Involves the *lower* lip nearly always.
Local symptoms.	A painless elevated papule, fissure, erosion, or ulcer. Regular outline, smooth surface, and has indurated circumscribed edges.	A painful, irregular, ragged sore. Bleeds easily. If induration present this is irregular. Discharges a thick offensive material.
Course.	Develops in a few weeks, followed in two weeks by sub-maxillary glandular enlargement.	Development very slow: takes as many months as the chancre does weeks. Glands not affected for months after appearance of sore.
Effects of mercury.	Causes disappearance.	Mercury has no effect.
Microscopical examination.	Probably shows presence of *Spirochaete pallida.*	*Spirochaete pallida* absent.

Chancre of Tongue. Less common than the former, involves the anterior half and may be found on the dorsal surface, the sides, or the tip.

Appearance. (1) Usually as a superficial erosion seated on an indurated base, surface smooth, covered very often by a grey false membrane. This may measure as much as half an inch across. (2) As a deep ulcer with sloping edges situated on a dense induration. (3) Simply as a dense sclerotic mass with unbroken surface.

Chancre very often simulates an ulceration caused by a carious tooth.

Chancre of the Tonsil is rare and is always difficult to diagnose owing to accompanying inflammation, and to the fact that the tissue in which it is situated differs so much in individuals. The chancre will at first closely imitate the original appearance of the tonsil, whether rough or smooth, being primarily an exaggeration of the natural condition due to hyperaemia or hyperplasia of the parts. The tonsillar chancre may be erosive or ulcerating. As an erosion it presents the appearance of a mucous patch, and is generally single. Induration may be made out by palpating with one finger in the pharynx and the other on the side of the neck. When a chancre of the tonsil assumes the ulcerating variety, the ulcer is deep, with abrupt edges embedded in an indurated mass. In chancres of the tonsils there is generally a history of a prolonged sore throat.

Diagnosis. The points which may help to differentiate tonsillar chancres from ordinary throat affections are—(1) they are unilateral, (2) their indurated character, (3) the presence of persistent indolent glandular swelling under the sternomastoid muscle.

Ocular Chancre. Chancres of the eye occasionally occur, although they are rare. They may be palpebral or conjunctival, and may be situated on either eyelid. Contagion may be indirect, by the fingers, by spitting, or by a contaminated towel. Surgeons are liable to these chancres, contagion having been conveyed in the course of examining the throat or mouth of a patient suffering from secondary syphilis. I have known the case of a medical man who contracted an ocular chancre during the course of an operation, some infected matter having found its way into the eye. This eventually turned out to be one of the worst cases of syphilis I have ever seen, mainly, I think, because, the lesion being unrecognized, the disease was for some time untreated.

An ocular chancre generally begins as a papule which gradually becomes indurated, then eroded, and sometimes ulcerated.

The glands in the vicinity of the ear and at the angle of the jaw become indolently enlarged in the first two weeks. Chancre of the palpebral margin has often been mistaken for a stye, a mistake which may be avoided by observing the development of induration and glandular enlargements which are associated with the chancre. Induration is always well marked in ocular chancres, and they are always accompanied by painless and hard enlargement of the pre-auricular, as well as of the cervical glands. Conjunctival chancres may be situated either on the palpebral or ocular conjunctiva, more often on the former, in which case the eyelid is everted and there is conjunctivitis and chemosis. The chancre is nodular, round, or oval, and may be erosive or ulcerating.

Facial Chancres may occur as the result of contagion from kissing, spitting, or razor cuts. The latter is not an uncommon cause. The cut, having healed, re-opens, and becomes covered with crusts, cracks around the mouth may persist, these are painless and become surrounded by a well-marked indurated areola ; erosion and ulceration takes place, the surface exuding a thin sanious discharge. Soon the sub-maxillary and parotid glands become indolently enlarged.

Chancres of the bearded cheek and chin may be mistaken for sycosis or eczema ; however, the circumscribed and indurated condition of the chancre with the accompanying enlargement of the glands, will help to differentiate it from other affections, and in the case of sycosis the trichophyton will be found.

Digital Chancres. Chancres about the finger are commonly found among medical men, dentists, and midwives. They may arise in any one, and have been conveyed by bites, &c. They may be of an eroded or ulcerated kind, most commonly the former. In these chancres induration is well marked and extensive. Sometimes the chancre may develop so insidiously, and look so like a small indurated papule, that it hardly attracts the patient's attention, and may thus remain unrecognized until secondary symptoms appear. Others develop into a large, hard, fleshy mass, purplish in colour, the surface being soft with exuberant vegetations on it.

One particular variety which is quite common, very much resembles a whitlow. The terminal phalanx of the finger is red, swollen, painful, and sensitive, and all the surrounding tissues are indurated. The ulcerated surface is rough and irregular, exuding a colourless fluid. This form of chancre is very slow in its development, and is remarkable for its long duration. The nail nearly always separates from the finger, and in a large proportion of cases the bone necroses. It may be very painful. It is to be noticed that most *digital chancres are remarkably painful.*

Adenopathy. In these cases the axillary glands are indolently enlarged. Any painless lesion about the finger, giving a scanty discharge, which slowly enlarges, and becomes hard, should always excite suspicion, and a watch ought to be kept on the adjacent lymphatic glands.

Vaccination Chancre. This form of chancre is much more rare now than it was when arm to arm vaccination was in vogue. If the vaccination 'takes', the resulting pustule may seem to be quite normal and heal up before any signs of a chancre appear; or the healing of the vaccination ulcer may be delayed. It presents a smooth surface, exudes a scanty discharge, is painless, and induration develops round it. The glands anatomically related to this part become enlarged and nodular. If the vaccination does not 'take', a characteristic chancre forms, beginning either as a papule or erosion.

Chancre of the Breast is usually caused by a syphilitic infant being nursed by a healthy woman. The lesion may appear either on or about the nipple, or in the integument covering the mammary gland. The former is the favourite site. It may commence as a fissure, crack, or erosion, and is often very difficult to diagnose. If these slowly extend, accompanied by little or no pain, exude a scanty, sanious discharge, and finally become indurated, accompanied by non-inflammatory enlargement of the glands in the axilla, a diagnosis of chancre can be made. Naturally the mouth of the infant should be thoroughly examined for secondary lesions.

Chancre of the General Integument. Chancres may occur at any part of the body which has been exposed to syphilitic inoculation, and the sources of contagion may be innumerable, but one source may be mentioned specially—tattooing has often been the cause of conveying contagion.

Prognosis of Chancre. Generally at the end of three or four weeks the chancre becomes cicatrized and the induration disappears, leaving a brown scar which may remain for years. This scar eventually loses its pigmentation and becomes white. The healing will, of course, be influenced very much by treatment—I mean constitutional; but chancres will heal spontaneously even when there has been extensive ulceration. There is seldom any deformity left, since any destruction of tissue is at the expense of the syphilitic infiltration, so that it is more apparent than real. Deformity will often follow a chancre which has been attacked by phagedaena, or when the ulceration—which is rare—has eaten through the induration into the adjoining tissues. Chancres situated in certain parts may give rise to other severe and oftentimes lasting complications. Chancres of the tongue or tonsil may cause grave difficulty of mastication; chancres of the conjunctiva, severe ophthalmia; and chancres of the urethra, stricture.

The question as to whether any relation exists between the source of infection, the chancre, and the constitutional disease of which it is a precursor, is one which has from time to time led to much discussion. However, the following clinical facts appear to be settled: (1) it is impossible to predict the form of chancre which will follow from a certain source of infection, as a different form may be acquired from one and the same source in different individuals; (2) my own experience is that to a 'certain extent' the severity, or otherwise, of the constitutional disease bears a distinct relation to the form of the primary chancre, and that an ulcerating sore is more often the prelude to one of the severe forms of eruption than is the ordinary dry papule; (3) a short primary incubation followed by a well-marked indurated lesion, and by a short secondary incubation, denotes the probability of a severe case.

Primary Lymphatic Enlargements are coincident with the development of the chancre. Usually at the end of the first week, or the beginning of the second, after the first appearance of the chancre, the lymphatic vessels leading from the chancre can be felt enlarged, and feel like a piece of cord under the finger. As a rule, this hard enlargement is quite painless, and there is an absence of any inflammation round it. This lymphangitis is most marked in genital chancres situated on the penis. At the same time as the above, and in connexion with these vessels, the associated glands become painlessly enlarged. The glands thus affected are those in the immediate neighbourhood of the chancre —in genital chancres the inguinal glands are enlarged; in chancre of the lips, the sub-maxillary; in chancre of the tongue, the suprahyoid and sub-maxillary; chancre of the eyelid involves the pre-auricular, and chancre of the fingers the axillary glands. The amount of enlargement of these glands is never very great, seldom exceeding the size of a marble. They are hard, indolent, painless, and freely movable. They never suppurate unless there is a mixed infection. It is only on the rarest occasion that a chancre is not accompanied by these enlargements of the lymphatics and accompanying glands. Hence their importance in the diagnosis of a chancre. At the same time it must be remembered that the lymphatic vessels and glands are also liable to become enlarged as the result of the presence of a chancroid, herpes, or any other form of non-specific sore. The following points will help to differentiate between the two :—

(A) *Specific lymphangitis.*	*Inflammatory lymphangitis.*
Symptoms.	
Hard, painless, non-inflammatory cord leading from chancre. No heat, redness, or tenderness.	Hard, painful, tender, and red cord: skin over it oedematous.
Termination.	
Resolution under specific treatment. Not affected by local treatment.	Often ends in suppuration: not affected by specific treatment, but is by local.

(B) *Specific bubo.*	*Inflammatory bubo.*
Number.	
Generally several (if genital) on both sides.	Usually *one* gland and confined to *one* side.
Symptoms.	
Small, indolent, painless, and movable.	Large, painful, tender: acute inflammation, redness and heat
Termination.	
Resolution: *local* treatment has no effect, *specific* has.	Generally suppuration: *specific* treatment no effect, but improves under *local.*

Treatment of Chancre. Persistent efforts have been made from time to time to stop the development of the disease by radical destruction of the chancre. The reasonableness of success in these efforts is, on *a priori* grounds, so great that the probability is that they will never be wholly abandoned. The actual results have been disappointing to a degree. The destruction of chancres by excision, chemical means, and the actual cautery, has repeatedly failed, not only to relieve the local symptoms, but also to prevent the recurrence of general symptoms. There is to this day a certain amount of division among authorities on the question whether the initial sore is merely a local point from which, after sufficient multiplication, the organism of the disease or its toxin is swept through the general system, or whether the chancre is the local expression of an intoxication generalized from the very beginning. This division of opinion is not likely to be knitted any closer by the discovery that *Spirochaete pallida* remains localised for such a short length of time—according to Metchnikoff one hour and a half, and to others much longer—at the point of inoculation before it begins its tardy move through the lymphatics to permeate the general system. It is quite possible, if not probable, that brilliant results may follow further attempts to destroy the spirochaete *in situ* at the beginning of the disease. And undoubtedly, from the prompt and extraordinary way the microbe disappears under the influence of mercury, applied either locally over the lesion containing it or otherwise, one cannot help being optimistic in the matter. As the question of the necessity, or otherwise, of the administration of mercury in the treatment of chancre will be subsequently discussed *in extenso*, it will suffice here to deal with the local treatment of the lesion. Locally, chancres should be treated by strict observance of the requirements of hygiene, and as a rule will require but little interference.

A chancre should be frequently washed with some antiseptic solution, such as 1 in 4 boric lotion, then dried well and dusted with powder, i.e. boric acid, europhen, aristol, calomel, and last, but far from least, iodoform pure and simple, without adding anything to it to take away its unpleasant smell. I have seen and used many substitutes, but have found them all inferior to iodoform. When the chancre is extensively eroded or ulcerated, it may be painted, after washing, with a solution of perchloride of mercury and tincture of benzoin to protect it from pyogenic infection, and for this reason a chancre ought always to be covered by medicated wool.

Salves and ointments should be avoided as a rule, the exception being when the discharge is thick and sticky. Cauterization is never required in an unmixed chancre.

The treatment of a sore complicated with phagedaena is far different; that most to be depended on is continuous immersion in hot antiseptic solutions. In the case of the penis this can be best carried out by immersing the member in some vessel, such as a bed urinal filled with the hot solution, and allowing it to remain there for lengthened periods. An ordinary hip bath may be used for the same purpose, but the immersion, however it is done, ought to be carried out thoroughly. Should the phagedaenic action continue, an endeavour must be made to destroy it by cauterization, either with chemicals or the actual cautery. The best application is chromic acid in the crude form. The patient must be placed under an anaesthetic or else the part rendered insensible by local anaesthesia. Then, the sore having been thoroughly dried, the crude chromic acid is applied to it; a black slough remains, which is detached by charcoal poultices, when, as a rule, a healthy surface is left; but it may be necessary to apply the acid again should the phagedaenic action still continue. Acid nitrate of mercury, as well as strong nitric acid, may be substituted for chromic acid, but in my experience they are not nearly so effective. Some cases of phagedaena may require the actual cautery. All phagedaenic sores need careful watching, as they are rapid in their progress and require prompt recognition and treatment.

CHAPTER XVII

THE INTERMEDIATE AND EARLY SECONDARY STAGES

The Period of Secondary Incubation. This is the period between the appearance of the chancre and the development of secondary lesions. Its average time is from forty to fifty days. During this time the chancre may have healed and completely disappeared, and the disease, so far as any constitutional symptoms are concerned, may appear quiescent. But, undoubtedly, during this time the virus is becoming disseminated throughout the entire system. This period of incubation is shortened in malignant syphilis and in constitutions which have been undermined by disease or excess, and is lengthened when the disease attacks those of robust constitution, or when it is of a mild type.

Evolution of Syphilis: the Stage of Secondary Symptoms. After this stage, and indeed during the stage itself, the virus of the disease manifests itself upon all the lymphatic glands not anatomically connected with the primary lesion, and the enlargement of these glands constitutes the earliest secondary symptom.

Enlargement of Lymphatic Glands not anatomically connected with the Chancre. It has already been seen that within a couple of weeks after the first appearance of the chancre, the lymphatic vessels and glands in its vicinity become enlarged and indurated; but this must not be confounded with the enlargement of the lymphatic glands now under consideration. In this stage the glands which have become enlarged are those situated in certain accessible regions, at least they can be more readily felt in these regions, and it is more than probable that all the lymphatic glands in the body sooner or later become affected. These accessible glands can be felt enlarged at about the sixth week after the first appearance of the chancre. This late glandular enlargement is pathognomonic of syphilis. The regions where these indurations can be best felt are the post-cervical, occipital, submaxillary, axillary, and the small glands situated over the mastoid process. These enlargements are hard, painless, and non-inflammatory. Of all the glands which become enlarged, perhaps the post-cervical and mastoid are the most pathognomonic. The former can be felt in a chain running down the outer edge of the trapezius.

With regard to the question as to what relation there is between the amount of this later glandular enlargement and the severity of a given case of syphilis, I do not think there is anything definite to be said, with the exception that the earlier this deep glandular swelling takes place the more likely the case is to be a severe one. But it must be remembered that some individuals are far more easily disposed to glandular swellings than others, for various and complex reasons.

Course of the Disease. The general or constitutional symptoms of syphilis are variously ushered in in different cases. In some there is well-marked fever, especially towards evening, and this may reach as high as 103° F.; when the eruption appears the temperature generally declines as in the case of the acute exanthemata.

Nocturnal Headache. Headache is another and very characteristic symptom at this period. It consists of more or less violent pains which shoot upwards along each temple, or of a dull ache running down the back of the head and neck. These pains are not felt during the day, but come on with surprising regularity towards evening, and become worse at night. At the same time osteocopic pains occur at different points over which there may be distinct tenderness, such as over the sternum.

One of the many points in which syphilis resembles the acute exanthemata is its strong tendency to affect the fauces. Indeed the throat sometimes suffers before any cutaneous eruption can be discovered, and in other cases an inspection of it reveals morbid changes which caused neither pain nor discomfort, so that the patient had no suspicion of their presence. The acute 'angina' of syphilis appears first as a diffuse redness. There is often a good deal of tonsillar swelling. The follicles become enlarged and prominent, or they may rupture, giving rise to shallow excoriations. In more chronic cases flat grey patches or ridges are present on the tonsils or palatine arches ; or there may be yellow ulcers with sharply-defined borders. But the most curious affection of all is one which is seen upon the fauces, hard palate, and inner surface of the cheek or lips. It consists of scattered milk-white spots called 'plaques', which are best compared with the effects of the application of nitrate of silver upon a mucous membrane. They may be of any shape and vary in size, and may run together so as to cover quite a large space. Sometimes they are slightly puckered, parts of their surface may be reddened with only a little white opacity here and there. These spots run a slow course and may break out again and again during a lengthened period.

Albuminuria. About this time also albumen may appear in the urine, the result of congestion of the kidneys.

*Early Skin Eruptions.** The next in sequence of events as the case goes on is the appearance of a skin eruption. Unlike all other specific poisons, the virus of syphilis produces not only one or two definite cutaneous affections, but an immense variety of them. They are known as syphilides or syphilodermata. As to the causes which lead to the evolution of any one of these eruptions rather than another we are in ignorance. All that can be said with any degree of certainty is that a patient who is in a bad state of health is more likely to develop eruptions which suppurate or ulcerate than he would otherwise have been, and perhaps that individuals predisposed to certain non-syphilitic skin diseases, such as ordinary psoriasis or lichen, are apt to be affected with a squamous syphilide, or with a papular one. At the same time syphilitic cutaneous affections are entirely distinct from the non-syphilitic eruptions which may simulate them.

There are certain features which belong, more or less, to all syphilides :—

1. Peculiar colour.
2. They are polymorphous.
3. Tendency to be disposed in circles or semicircles.

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* These will be more fully dealt with in the Section on the Skin in vol. v, to which the reader is referred.

4. Absence of pain or itching.
5. They are asymmetrical.

As regards their colour, this is said to be ‘ coppery ’, or ‘ raw ham ’. The cause of this tint is perhaps due to chemical changes in disintegrating blood corpuscles which have been extravasated into the tissues.

The *second* character of syphilitic skin affections is their multiplicity or ‘ polymorphism ’ in the same patient and at the same time. Sometimes macules, papules, pustules, and scaly patches are so intermingled that it is impossible to say which preponderates.

The *third* point is their tendency to arrange themselves in circles, semicircles, or annular forms.

Syphilitic skin affections are, as a general rule, quite free from any subjective symptoms, such as pain or itching ; in many cases patients experience nothing whatever to draw their attention to the skin, and the eruption is only discovered by accident, as it were.

The *fifth* point is that they are asymmetrical. The first rash may be symmetrical because it affects the symmetrical human body, but syphilides do not show the characteristic symmetry of psoriasis, eczema, and some other cutaneous diseases in picking out corresponding parts of the trunk or limbs. They are irregular in distribution : their favourite localities are the forehead, the sides of the feet, and the palms of the hands, and they often affect regions rarely visited by other cutaneous affections.

In most cases, however, a correct diagnosis must be based not so much upon the recognition of those characters which are common to all syphilides as upon an accurate acquaintance with each of them individually. It is, therefore, absolutely necessary that they should be classified. The general division of syphilides is into those which appear early and those that show themselves late. The former make their first appearance very rarely beyond the first twelve months of infection. The latter seldom appear within the first year, and their appearance may be postponed for several years.

The later syphilides are known as tertiary.

Classification of Early Syphilides

I. Erythematous, or macular.
II. Follicular
  - Lichen.
  - Acne.
III. Papular (lenticular)
  - (*a*) Psoriasis.
  - (*b*) Mucous patches.
IV. Squamous.
V. Vesicular.
VI. Pustular syphilides.

I. *The Macular Syphilide* (*roseola*) (see Plates XL and XLI). This is the earliest and most common of all the skin eruptions of syphilis, coming out about the same time that the general lymphatic enlargement becomes apparent. It consists of pale, or dark-rose, or 'copper'-coloured spots, irregular in form, and small in size—about a third of an inch in diameter—scarcely raised above the surface, and generally disappearing entirely on pressure.

This form of eruption is usually seen on front of the chest, abdomen, and sides of the chest; also on the back of the trunk and neck. Sometimes it appears on the face, but this rarely; it is more common on the flexor surfaces of the limbs, but it avoids the hands and feet. As a rule it takes about a week to fully develop, but sometimes it develops so rapidly that it might be mistaken for measles. It remains for different lengths of time. A pale and scanty eruption often fades within a fortnight or less, whilst one which is dark-coloured and abundant may remain visible for weeks. It may then after a time assume a squamous or papular character. This syphilide is apt to relapse, and it may occur at any time during the first year and even in the second.

The later the macula relapses the larger the spots are.

II. *The Follicular Syphilide.* There are two varieties of this; one consists of small, pointed, dry elevations or papules, generally scaly at the summit, and their bases may be surrounded by a white desquamating cuticle.

They may be either irregularly scattered or occur in groups or clusters. This eruption is exceedingly slow in its course, developing itself by successive crops and subsiding after several weeks or even months. Sometimes the papules pass into pustules, and on disappearing they always leave minute white cicatrices.

The other variety consists from the first of pustules which, like the papules, are small and pointed, with swollen red bases. They may be present in immense numbers, not only on the face, but on the trunk, back, and chest.

III. *The Papular Syphilide* (*lenticular syphilide*). (Plate XLII.) This lesion consists of red, shining elevations. They feel hard and shotty, and vary in size from that of a millet seed to that of a good-sized pea. They develop very rapidly, coming out in a few days. They come out in crops over a period of some weeks. The eruption is scattered irregularly all over the body. They are sometimes numerous on the forehead and neck, and occasionally appear profusely upon the face. ('Corona Veneris,' Rondelet, 15th century.)

The papules remain for a long time—weeks and sometimes months—and then gradually disappear. At other times their summits soften down and become covered with a brown crust.

(*a*) On thick cuticle, like that of the palms and soles, the spots are not raised into papules, but form round horny plates with copper-coloured margins. After a time the plates become detached and their places are taken by thick crusts or scales, or an ulcer forms. This is the condition which constitutes 'syphilitic palmar, or plantar, psoriasis'.

(*b*) Mucous patches. Another variety of the papular syphilide is seen on the delicate parts of the skin which touch each other; also on the mucous membrane of the various orifices, their favourite sites being about the genitals, perineum, in the folds of the nates, on the axillae, between the toes, and the angles of the mouth. The affection consists of broad raised patches, which may measure an inch in diameter, with the edges sharply defined, the surfaces sometimes dry, but much more often moist, and coated with a dirty grey secretion which gives off a sickly odour. These lesions consist of cell-infiltration of the cutis with the addition of an overgrowth of the papillae. They sometimes become confluent, and then a large portion of the skin is involved. About the anus this affection assumes the form known as 'condylomata'. These appear as flat, raised, pale growths. They are due to a well-marked papillary overgrowth. Occasionally large, cauliflower-like excrescences are formed, especially about the genital region. These are termed vegetating papules. (Plates LIII and LIV.)

Condylomata, and, in fact, all syphilitic mucous patches, are highly infectious, and are probably more often the cause of spreading the disease than any other lesion. In them also the *Spirochaete pallida* can be more readily demonstrated than in any other material. (See Plate XIII.) The secretion from mucous patches often gives rise to warty growths beneath the prepuce, in the vulva, &c.

IV. *The Squamous Syphilide* ('*syphilitic lepra*'). These lesions are flat and hardly raised above the surface; they are covered with silvery scales, underneath which is a coppery glistening surface. The scales are easily detached and accumulate over and over again on the surface. The eruption comes out rather late; the spots are always scattered, are few in number, and are confined to one particular region—for instance, they may be limited altogether to the palms of the hands and the soles of the feet.

A particular variety—'the circinate syphilide'—is fairly common. The lesion assumes the shape of rings, and resembles very much *Tinea circinata*, but the exfoliation of the margins is generally profuse, and the silvery scales become easily detached. These rings are few and scattered, the favourite seats being the front of the thighs.

V. *The Vesicular Syphilide* is rare. The vesicles are, as a rule, small, may come out profusely all over the body or in groups, the face and genitalia being mostly the selected spots. The vesicles are filled with a clear fluid which usually dries up: on the contrary, they may become pustular. (Plate XLIII.)

VI. *The Pustular Syphilide* ('*syphilitic rupia*') consists of pustules of all sizes, each of which is seated on a firm base. They may be present in immense numbers, especially on the face and trunk. They come out rapidly and in successive crops, and are accompanied by much febrile disturbance. They may relapse even after a year. They dry up into brown or black scabs, and leave large stains, which ultimately pass into shallow, flat cicatrices. In other cases their inflamed bases continue to spread long after their summits have scabbed over. Thus, as the crusts increase in size, the older parts of them are continually being pushed upwards by the collection of fresh material beneath, the consequence being that they assume a conical shape and look like shells. Some of them acquire enormous size. This variety is what is called 'rupia'. It resembles the tertiary rather than the early syphilide, but as it is sometimes a very early eruption I describe it as such. (See Plates XLIV and XLV.)

Other Early Secondary Symptoms.[*]

Anaemia and Alteration in the Blood. Anaemia is generally a marked symptom in early syphilis. Even prior to the appearance of any rash, and accompanying the enlargement of the lymphatics not anatomically connected with the chancres, the patient becomes pale, listless, loses weight, and is evidently gravely debilitated. There is a general 'impress' about him which, to the expert, is always significant.

Alteration in the blood. On examination of the blood it will be found to be deficient in haemoglobin and red corpuscles, with some increase in leucocytes, but there is no distinctive feature in the blood count. These changes become more marked as the case proceeds. The intensity of the blood changes corresponds with the severity of the case (refer pp. 123–125).[†]

Early Visceral Affections. We have already seen that there may be albuminuria due to hyperaemia of the kidneys; so also there may be headache from meningitis, and pleural effusions from inflammation of the pleura. The liver also may become congested, causing jaundice.

Nervous System. (1) Syphilitic neuralgia has already been alluded to. This may be due either to general cachexia or to pressure from effusion.

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[*] These will be more fully dealt with in the special accounts of each System.

[†] The administration of mercury is said to be followed by a sudden fall of 10–20% of the haemoglobin. This has been used for diagnosis (Justus's test), but its efficacy is doubtful.

(2) Headache is common, and simulates more a feeling of increased tension than of actual pain. This feeling is generally located in the occipital region. Nocturnal exacerbations are marked.

(3) Paralysis, especially of the muscles of the eye and face, very often comes on quite early in syphilis. Hemiplegia and paraplegia are also not uncommon symptoms during the secondary stage, especially in untreated cases. The former is due, generally, to endarteritis or thrombosis of the middle meningeal artery, paraplegia to some meningitis of the membranes of the cord. Luckily, both these lesions, when they occur in early syphilis, are transient, and tend to disappear under treatment.

Chorea. Sometimes this is an early symptom, and generally accompanies partial hemiplegia. The movements are often confined to the arms.

Other Early Secondary Lesions of the Skin and Appendages.

Alopecia is a fairly early symptom, and is very common. There may be total or partial loss of hair. The former is rare, and when it does occur, there is a general shedding of the hair with resulting baldness. More commonly the shedding of the hair is irregular, it comes out in patches, leaving circular bare spots on the scalp. Syphilitic alopecia may attack the moustache, beard, or eyebrows. As a rule the hair grows again readily in syphilitic alopecia, unless there has been destruction of the papillae, in which case baldness remains permanent.

The nails. Onychia is due to the action of the syphilitic poison on the matrix of the nails. The latter become dry, brittle, and break on the least pressure. They may be cracked and fissured, and eventually they may loosen, and be shed. Sometimes the nails become discoloured and distorted. These affections are quite painless and non-inflammatory.

Paronychia. When the tissues about the nail are involved the affection is called paronychia. The latter may be dry or moist. Dry paronychia begins as an infiltration round the nail, and generally assumes the form of a papule, which involves the cutaneous fold, occasioning thickening and exfoliation of the epidermis. The nail becomes brittle and cracked. Moist paronychia is an ulcerating affection. It begins as in the dry form, but goes on to ulceration. An unhealthy ulcer, with exuberant granulations, forms about the nail, which it often undermines.

Early Secondary Affections of the Tongue. These consist of mucous, smooth, or scaly patches. Mucous patches are of an erosive type. They may consist of small red spots, fissures, or cracks. They are frequently situated on the side of the tongue, and are sometimes painful, but as a rule are not. The smooth patches appear on the dorsum of the tongue as smooth, shiny, reddish, flat patches. They are circular in form and are caused by desquamation of the epithelium. Sometimes they cannot be seen until the tongue has been dried by a towel.

The scaly patches are the most common ; they are grey-white in colour, circular in shape, often well raised above the surface of the tongue, especially when seated at the back of the organ, when they are papular. They are not, as a rule, painful except when irritated from smoking.

Early Secondaries of the Gums, Palate, and Uvula. The gums are often attacked with a form of pyorrhoea, and the palate and uvula with the usual macular erythema.

Secondary Syphilis of the Eyes. Among the early secondary affections of the eye, iritis takes first place. It is of two kinds : simple plastic, and parenchymatous iritis.

Plastic Iritis often occurs in about the second month of the disease. It is characterized by severe, supra-orbital pain, which is worse at night : contracted and sluggish pupils : discoloured iris : adhesions between the iris and lens and vascular injection of the circumcorneal zone.

Parenchymatous Iritis presents yellowish-brown nodules on pupillary border of an inflamed iris. These nodules are very distinct, and, together with the ordinary signs of iritis, go to form true syphilitic iritis.

Other Early Secondary Affections of the Eye consist of cyclitis, choroiditis, irido-choroiditis, and retinitis, but these are not very early secondary signs.

Early Secondaries of the Nose. The only really early secondary affection of the nose is the presence of moist papules about the nostrils.

Early Secondary Affections of the Bones. The osseous system is often one of the earliest attacked by syphilis. The disease begins as simple periostitis running on sometimes to inflammation of the bone itself. The tibia, sternum, clavicle, bones of the cranium, and ribs are most frequently attacked, and in the order named. Periostitis is often a very early secondary affection, which sometimes appears even before the appearance of any rash; it generally develops, however, between the sixth and ninth months. It is a sub-acute affection. Examination shows a swelling over one of the above-named bones which is elastic, tender, and painful; the pain is often intense, especially at night time. Under treatment this latter will gradually subside, leaving no trace behind; but sometimes the bone itself becomes engaged, when the inflammation is sometimes followed by suppuration, in any case bony nodules, called osteophytes, remain at the seat of the attack.

Early Secondary Affections of Joints. The joint affections of early syphilis are two: acute and sub-acute. The former generally attacks the elbow joints, both at the same time. There is slight swelling accompanied by severe pain, which is always worse at night time, and there is always a marked rise of bodily temperature, which may be as high as 104° F. Under treatment this joint affection generally ends in resolution.

The sub-acute—which is far more common than the acute—very often attacks one knee only. There appears a swelling of the joint unaccompanied by much pain. There is little bodily disturbance, and the amount of pyrexia is insignificant. It generally ends in resolution.

Bursitis. The bursae may also become acutely inflamed as an early secondary lesion, but this is rare.

Muscular Rheumatism, in the form of an irritative myositis, often comes on very early. The muscles chiefly attacked are the biceps and triceps. In them there is dull pain which is aggravated by pressure or motion. Sometimes they are painfully contracted.

Affections of the Tendons. Teno-synovitis may come on at an early stage and is characterized by effusion, tenderness, and swelling along the course of a tendon, sometimes only one, such as the tendo Achillis, is affected; at other times it attacks several tendons at the same time, and there may be severe pain and tenderness over them.

Early Secondary Affections of the Epididymis and Testicle. These are not common, the testicles being more commonly the seat of tertiary syphilitic lesions. The early affection appears as an acute epididymitis and under treatment always ends in resolution. Early secondary orchitis is very rare, and is usually an accompaniment of the epididymitis. It follows the course of ordinary acute orchitis and resolution is generally the result.

The Treatment of the Early Secondary Lesions of Syphilis. In considering the question of the treatment of early secondary affections, it may be stated at once that, as they are the symptoms of a constitutional disease, they will require to be attacked from that point of view from the very beginning.

All authorities are agreed that there is only one drug which possesses the power of curing syphilis, i.e. mercury, which is consequently our sheet anchor at any and every stage of the disease, and that without its exhibition all attempts at curing the disease will be fruitless.

All other medicaments are merely useful adjuncts when dealing with the disease. As the subject of the general treatment of syphilis will be found fully discussed in a later part of this work (vol. ii), I do not propose to allude to it in this chapter, confining myself altogether to the local treatment of the early secondary lesion, taking it for granted that mercury is being exhibited at the same time.

Early nocturnal headache is best relieved by iodide of potash given in 5-gr. doses three times a day. The salt sometimes acts like magic in these cases: local treatment is useless.

Mucous Patches in the Mouth, Inner side of the Cheek, Tongue, &c. Before entering into the question of the local treatment of these lesions it is necessary that some remarks be made as regards the hygiene of the mouth. In the case of all syphilitics the greatest possible attention should be paid to this.

Prior to the commencement of any treatment, if possible, a visit should be paid to a dentist, all old stumps extracted, and the teeth kept in as perfect order as possible. The teeth should be brushed frequently—after each meal at least, and some antiseptic tooth-powder used. The gums should be thoroughly examined, and, with a view to keeping them in good condition, an astringent mouth-wash should be used frequently during the day. A very good one is as follows :

1. Plumbi acetatis, ℥i.
   Aquam, ℥v.
2. Aluminis sulphatis, ℥i.
   Aquam, ℥v.

These two solutions should be mixed and filtered, and to the filtrate is added ten parts of water and a few drops of some aromatic essence. This is the mouth wash which is generally used at Aachen; the patients carry a bottle containing it about with them, and use it very frequently during the day. If mouth-washes are objected to, tabloids of chlorate of potash may be sucked, or the gums painted two or three times a day with tincture of myrrh or peroxide hydrogen. Smoking should be either forbidden altogether or allowed only to a very limited degree. Smokers are ten times as liable to suffer from mucous patches and ulcers of the mouth and tongue as non-smokers. The importance of doing everything to preserve the health of the mucous membrane of the mouth cannot be too strongly insisted on, as upon it depends to a great extent the ability of the patient to take a sufficient quantity of mercury without causing salivation. As regards the mucous patches of the mouth and tongue these should be touched daily with a strong solution of nitrate of silver, or with a solid stick of the same. For the scaly patches, by far the best application is chromic acid, from 10 to 20 grs. to the ounce, with which they should be touched at least every second day, or after being so treated the solid nitrate of silver may be applied over the chromic acid solution, thus forming chromate of silver. Some authorities prefer to treat these lesions with applications of acid nitrate of mercury. Should the patches persist, they should be removed by a sharp curette and then treated on ordinary surgical principles.

Ulcerated patches in the throat should be treated in a similar way. Here antiseptic sprays and gargles are most useful, Mauriac recommends fumigation :—

℞
Cinnabar, 15 gr.
Hydrarg. iodidi virid., 7 gr.
M
Signa. For one fumigation lasting twenty minutes.

An excellent application for all mucous patches of the mouth, tongue, and throat is Perhydrol (Merck, Darmstadt). Perhydrol represents a chemically pure aqueous solution containing 30 per cent. by weight H_2O_2 : ordinary peroxide of hydrogen containing only 10 per cent. H_2O_2. The former is absolutely free from acid and is non-irritant ; it can be used concentrated or diluted to any strength. It is absolutely non-irritant, and in the author's hands has proved most beneficial. The ordinary peroxide is not reliable, as its strength is uncertain, and it is decidedly an irritant.

In any persistent ulceration of the throat and upper part of the pharynx, too much stress cannot be laid on curetting. This should be done boldly and thoroughly to prevent any permanent injury. With the aid of a local anaesthetic it is very easily carried out. The author has latterly been in the habit of using the curette much earlier and more extensively in all mucous patches and ulcerations than hitherto, and with the best results. Various authorities recommend different applications in the local treatment of early syphilitic lesions of the mouth and throat, but taking them in order the writer thinks that it will be found that the best are chromic acid (10 to 20 gr. to the ounce) ; chromic acid solution followed by the solid stick of silver nitrate ; acid nitrate of mercury ; and finally—although it is not exactly an application —curetting.

If any other reason may be required as to the absolute necessity of keeping syphilitic patients as much as possible in the open air whilst under treatment, it is furnished by the fact that both mucous patches and syphilitic ulcers are much accelerated by confinement indoors, hence for this reason alone the keeping of patients in the open air as much as possible ought to be insisted on.

Local Treatment of Condylomata. The best application for these lesions is strong nitric acid, and after this comes acid nitrate of mercury and chromic acid. The acid should be applied on a match-stick, never on a glass rod, as when the latter is used the caustic is liable to run.

When condylomata are very extensive they should be curetted freely and treated on general surgical principles.

In the lesions known as vegetating papular, or ulcerating granulomata (see Plates XLVI, XLVII), the best line of treatment is free curetting, followed in a week or two by exposure to the X-rays.

Local Treatment of Skin Lesions. Erythematous syphilides as a rule require no local treatment. However, should they be very conspicuous and persistent, the following application may be found useful :—

℞

Hydrarg. chloridi, ʒi.
Ung. zinci oxidi.
Ung. paraffini carbolici (20 per cent.),
aa ℥ss.
Sig. Apply locally.

Or a powder containing calomel with starch may be dusted over the parts.

All cutaneous syphilides are benefited by hot baths, hot-air baths, and vapour baths, and this is another reason for the *systematic employment of baths* in the general treatment of all cases of syphilis.

Papular syphilides are sometimes much benefited by the application of ointments containing mercury, such as

℞

Ung. hydrarg. nit.
Paraffin carbol. (20 per cent.) aa ℥ss.

or,

℞

Hydrarg. ammoniat. ʒi.
Ung. aquae rosarum, ℥i.

Papulo-squamous eruptions of the palms of the hands and soles of the feet are much improved by being dabbed daily with

Perhydrol (Merck) in the concentrated form. This the writer has found to be a great boon, as these lesions are not only unsightly but generally very persistent, and consequently are always a source of anxiety to the patient.

Usually much more can be done by local measures for tertiary skin affections than for the early secondary, but these do not come within the scope of this section.

Plates XLVI and XLVII illustrate a rare condition known as Ulcerating Granuloma; although not strictly an early affection of syphilis the rarity of the condition would seem to justify an account.

Ulcerating Granuloma. Private B——, age twenty-five. History. Contracted syphilis in 1902, for which he was then in hospital for three months. Two years later, whilst in India, he was again in hospital with condylomata and mucous ulcers in the mouth, which disappeared under specific treatment, but these recurred six months later, and he was again in hospital; the condylomata are described as having been 'an immense crop resembling bunches of grapes'. Specific as well as all other forms of treatment failed to make any impression on them, and seven months later the patient was invalided home to Netley, where he remained under different forms of treatment (including two courses of Zittmann's) for three months, when he was sent to the Military Hospital, Rochester Row, London.

Condition on admission. General health very good, no symptoms of syphilis beyond the local condition, and this did not appear to have caused any suffering, either by its severity or the prolonged course of treatment it had necessitated. Local condition: There was a large fungating mass of granuloma around the anus, extending a hand's breadth on to the buttocks on either side and forward on the perineum to the base of the scrotum. The mass had broken down in the centre, leaving a craggy crateriform ulcer about three inches across and an inch deep, at the base of which the mucous membrane of the anus could be seen; this did not appear to be affected. The sphincter was not implicated, and the patient suffered little discomfort, except in the act of defaecation. The margin of the mass was marked by a series of ovoid shallow ulcers, and all the parts affected were deeply congested and presented a sodden and thickened appearance gradually fading off into the normal tissue. Both *Spirochaete refringens* and *S. pallida* were demonstrated in smears from this ulcer.

Treatment. Mercury by mouth, inunction, and intramuscular injection. Potassium Iodide. Iodoform by subcutaneous injection. Arsenic. Local applications of all sorts, including chromic acid. Acid nitrate of Mercury, Peroxide of hydrogen and baths. The only treatment which had any effect was Mercury, and benefit was received from this drug. The specific treatment caused the offensive odour and discharge to disappear, with a certain healing up of the ulcer, although a cure could not be effected by it. The condition responded more to intramuscular injections of calomel than to anything else. The patient went through an X-ray course at Charing Cross Hospital, having an exposure once a week to 6000 (v), for a period of three months. At first the condition appeared to improve, but he gradually relapsed, the discharge and odour returning. Eventually, on March 19, 1907, the patient was put under an anaesthetic, and the whole mass scraped away with a Volkmann's spoon, but this was done with difficulty, the growth being firmly attached; however, it was eventually cleared away. There was considerable capillary bleeding. The base of the scraped surface was very hard with a parchment-like feel, and did not seem likely to granulate; however, this it did in the most remarkable way, and the patient left hospital cured in less than a month after the operation, and up to date has had no recurrence either of the local condition or constitutionally.

Remarks. This was evidently a case of what one frequently meets with in the Tropics among syphilitic patients (W. India, British Guiana, and Uganda), and it has been described as 'Ulcerating Granuloma'. Personally I have little doubt that the condition is the result of some other infection peculiar to those regions, attacking syphilitic lesions, but which is quite foreign to the syphilitic infection, hence the failure of specific treatment to effect a complete cure.

The treatment of such cases is, besides specific treatment, total extirpation of the granuloma. I have little doubt but that the patient under notice had been practically free from syphilis for some time.

F. J. Lambkin

Plate XXXIV.

Chancre on the corona of the glans penis.

PLATE XXXV.

Initial manifestation of syphilis at the point of reflection of the epithelium covering the glans penis and the prepuce.

Plate XXXVI.

Initial manifestation of syphilis, showing extra-glandular circumscribed induration.

Plate XXXVII.

Penile chancre, showing extensive ulceration, induration being almost completely destroyed.

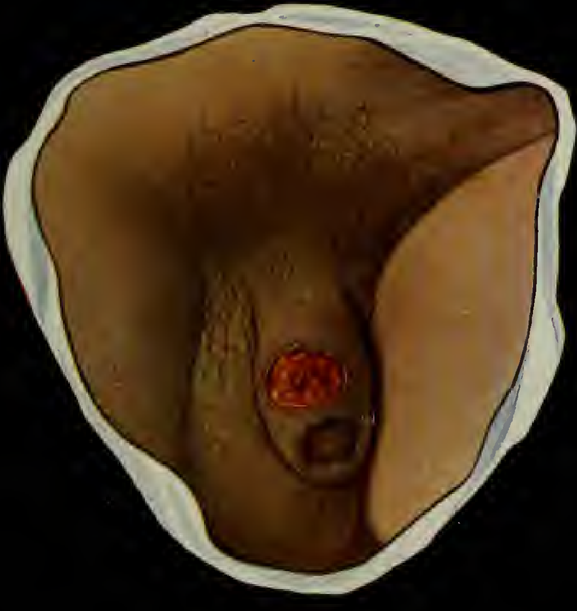


Plate XXXVIII.

Chancre of the prepuce (preputial).

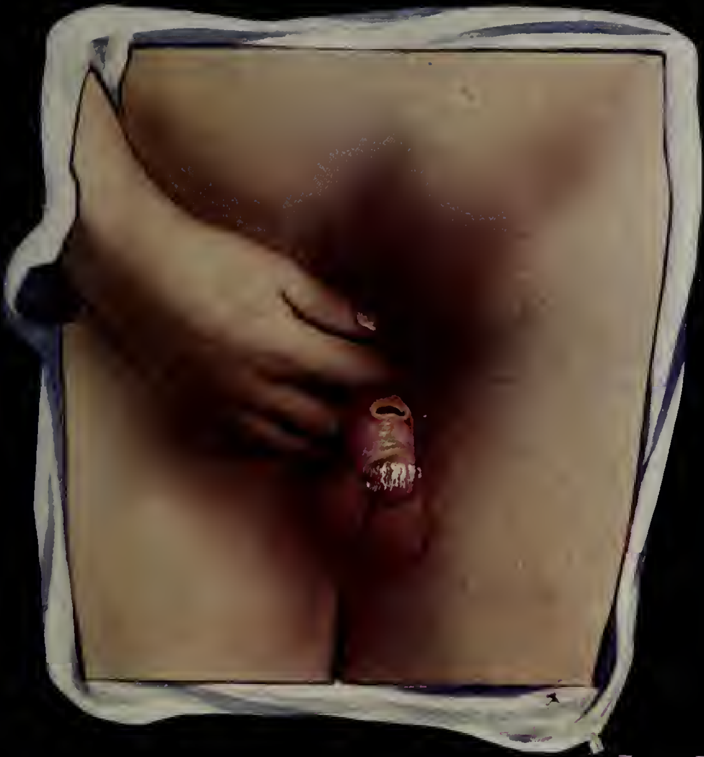


Plate XXXIX.

Phagedaenic chancres of the groin, from a case of mixed infection with buboes.

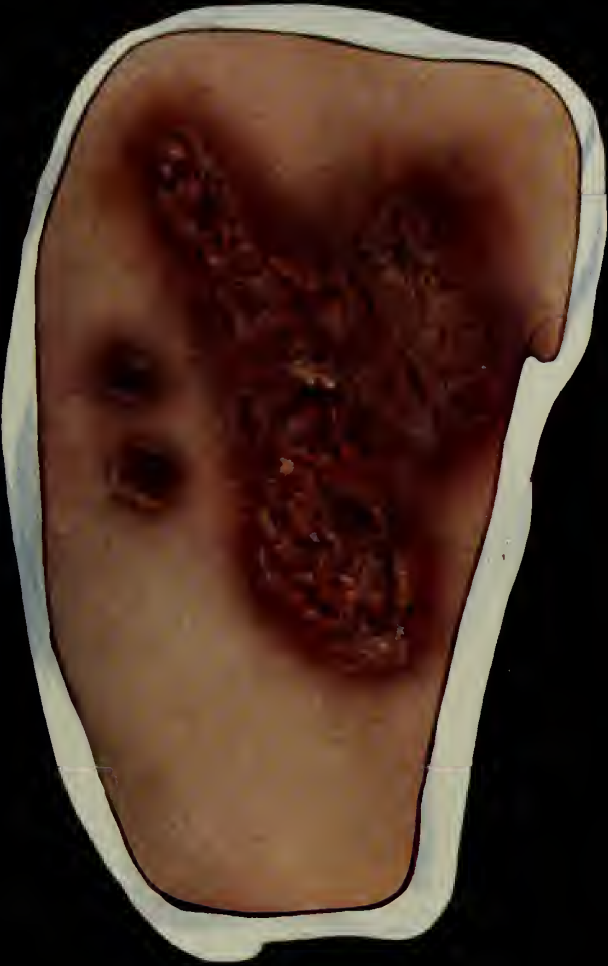


PLATE XL.

Early macular secondary eruption.

(From a direct colour-photograph.)

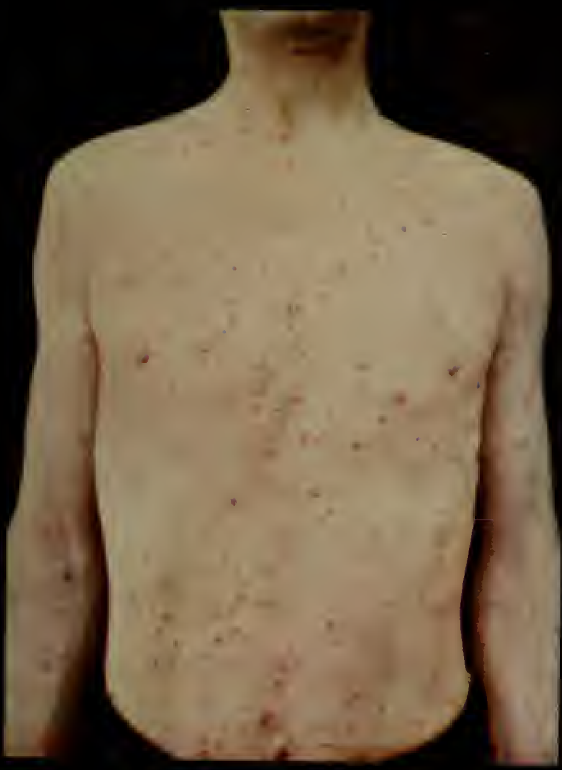


Plate XLI.

Early roseolar eruption (female).

(*From a direct colour-photograph.*)

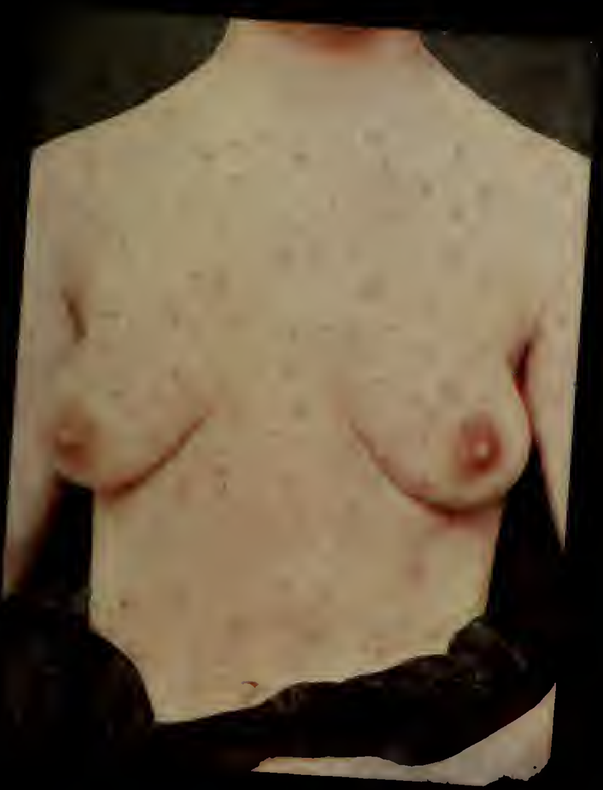


Plate XLII.

Profuse early papular eruption on back.

(*From a direct colour-photograph.*)

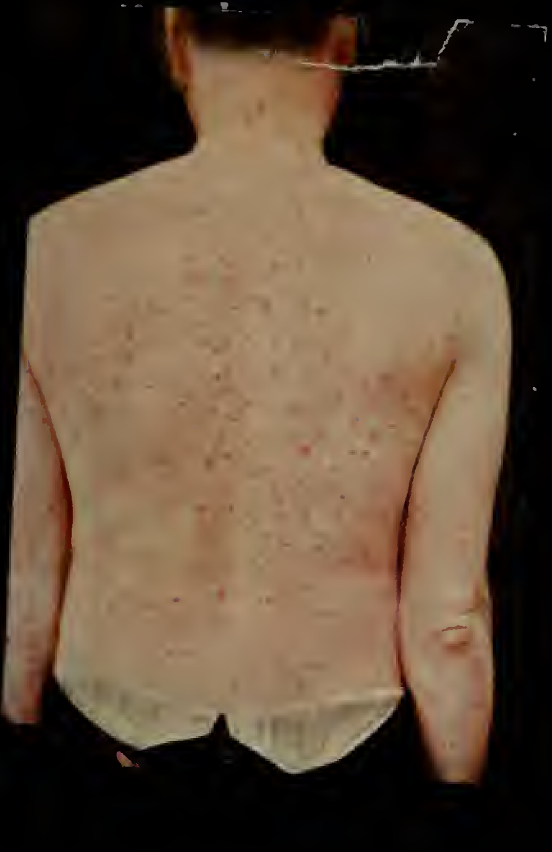


Plate XLIII.

A vesicular eruption on the chest and abdomen, occurring eight weeks after infection with syphilis.

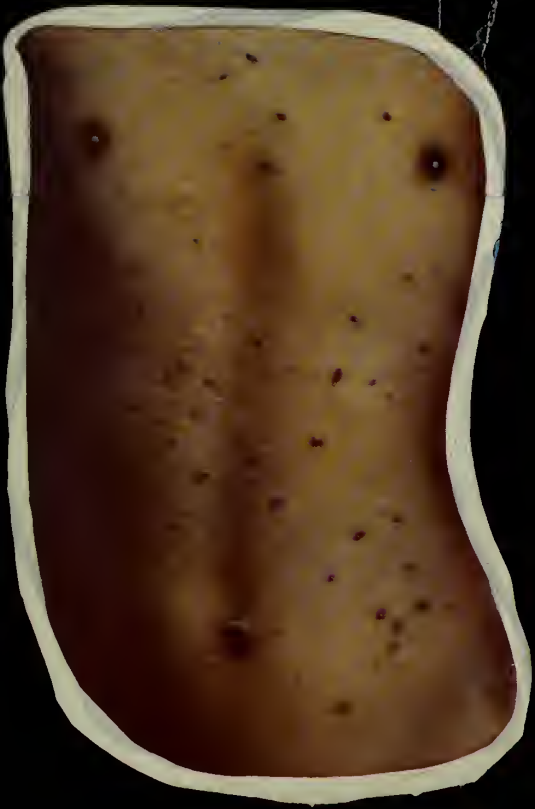


PLATE XLIV.

Abortive pustular eruption.

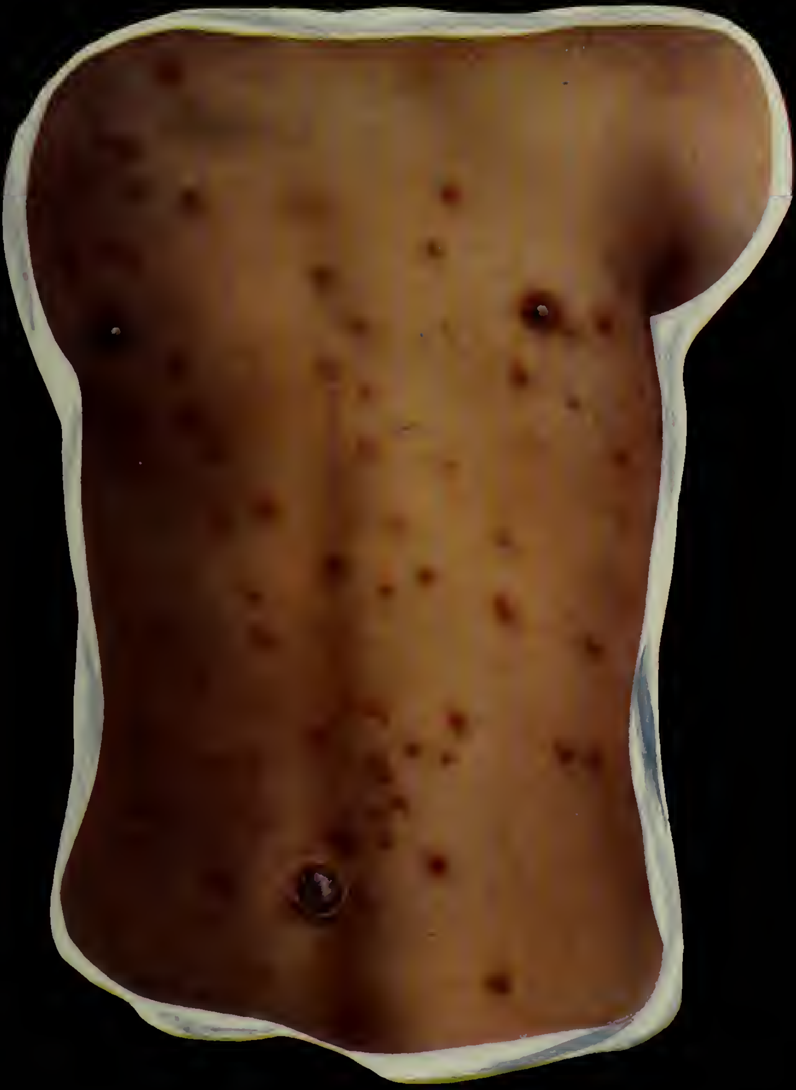


PLATE XLV.

Papular eruption, tending towards rupia, occurring seven months after infection.

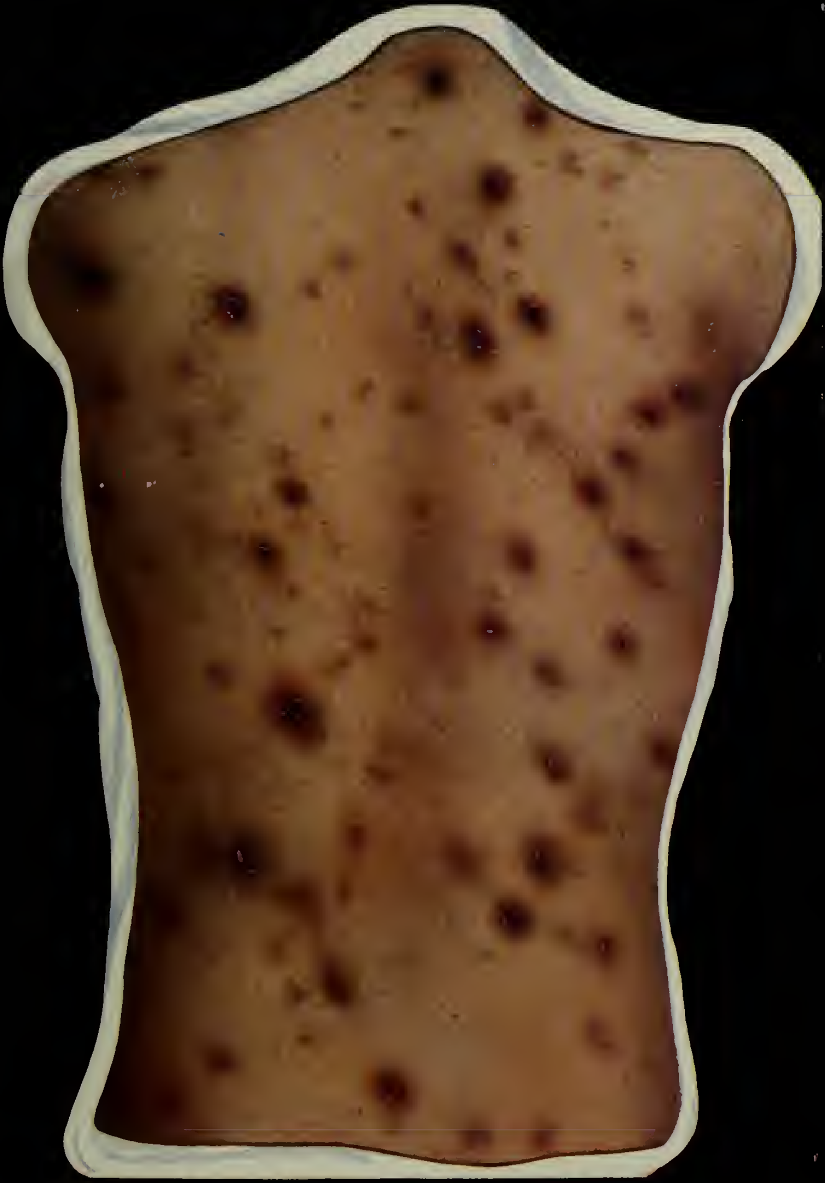


Plate XLVI.

Ulcerating granuloma (syphilitic) of the anus. Three years after primary infection.

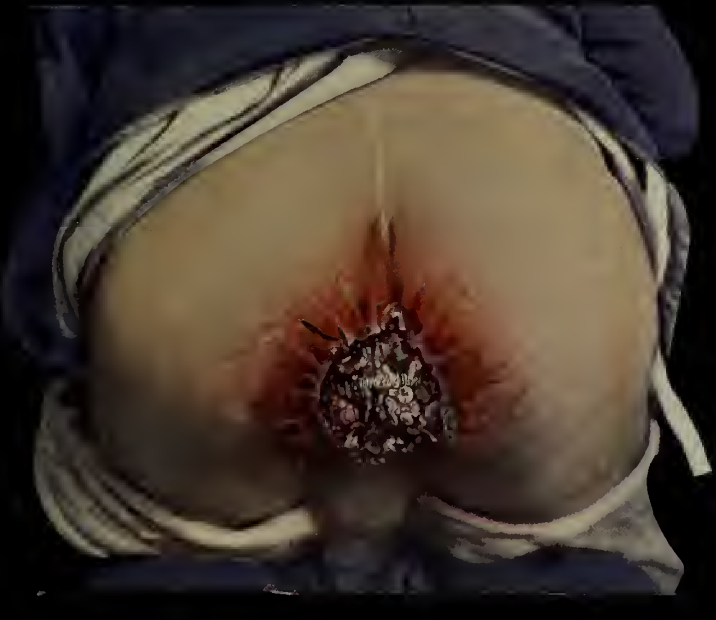
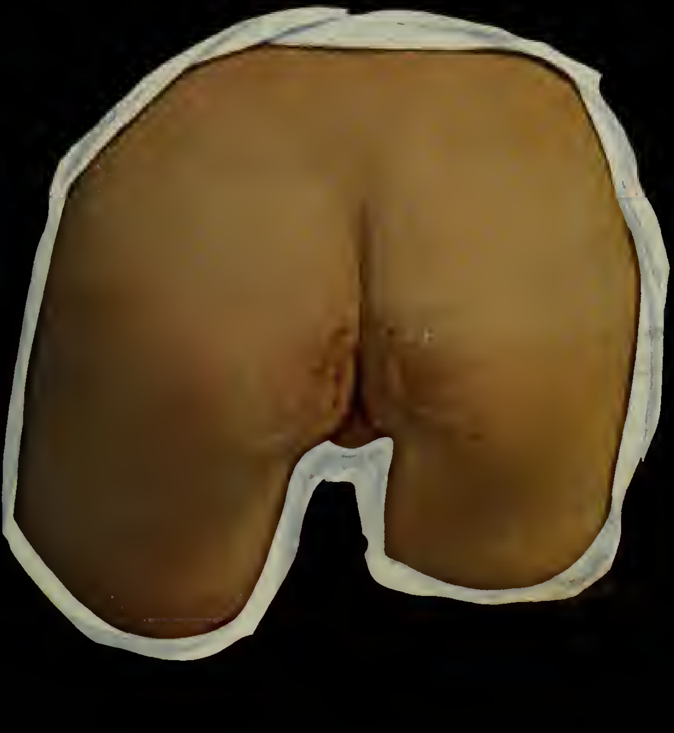


PLATE XLVII.

Same case as that of preceding plate, one month after removal of granulomatous mass.



THE PRIMARY LESIONS AND EARLY SECONDARY SYMPTOMS, AS SEEN IN THE FEMALE

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CHAPTER XVIII

INITIAL GENITAL LESIONS

GENERALLY speaking, much greater difficulties will be met with in arriving at a correct diagnosis, with respect to the initial lesion, in women than in men. Many factors combine to bring about this state of affairs.

Compared with the knowledge of the disease possessed by men, very many women are absolutely innocent and altogether ignorant of the serious nature of the complaint. Indeed, it not infrequently happens that we are asked to, and do, treat a woman for the whole course of the disease without perhaps once mentioning the word syphilis, or giving her any inkling as to the true nature of the ailment from which she is suffering. In by far the majority of cases it is impossible to discuss the conditions in the same open way as with men. Thus, much greater difficulty is experienced in obtaining a reliable history, or in arriving at the true facts of the case. In addition to this, the genitalia being anatomically different as well as more complex than in men, the difficulties of a thorough examination are increased, with the result that the initial lesion much more frequently escapes discovery than in the opposite sex.

But perhaps the chief difficulty met with is the fact that often no obvious primary lesion is found present, however careful and minute the examination.

Owing to its situation and general environment the primary lesion is less exposed to friction and other causes which tend to prolong the existence of the chancre in men ; again, the conditions under which it exists, being favourable to its earlier healing and complete resolution, render it impossible in very many cases to say at what point the virus has effected an entrance. One not infrequently learns, when endeavouring to obtain from a patient, the subject of secondary syphilis, points bearing upon the history of the case, that she, perhaps as early as the day following the last intercourse, had noticed a small chafe or tear. That this had either disappeared spontaneously or had yielded to some simple treatment, and had been regarded as of no importance whatever. The patient, in spite of constant examination, seeing nothing for several weeks, will have believed that she has escaped infection, until the onset of secondary lesions has convinced her to the contrary.

The following case is an illustration of this difficulty :—

Case 1. ——, aged 23, single, was admitted into the hospital under my care with an oedematous condition of both labia majora ; the surface of each labium was ulcerated and discharged freely. The swelling of the labia was of an inflammatory type rather than that of the primary indurated oedema so often found affecting these parts. There was double adenitis in the inguinal and posterior cervical regions, the glands being hard, smooth, painless, and discrete. There was a papular eruption over the posterior and lateral aspects of the neck as well as on the abdomen. (See Plate XLVIII.)

The patient assured me that she had kept a most careful watch over herself, and she was quite positive that the eruption appeared some days previous to the vulval condition, which had only been present a fortnight.

In such a case, I think, we may quite reasonably assume that the original lesion was of the ephemeral type ; that it had cleared up rapidly, and so escaped notice. But, as we not infrequently see, with the onset of secondary symptoms it had relapsed, and that the induration had been dissolved by the septic condition the parts had been allowed to get into.

This ephemeral nature of the initial lesion is very much more common in women than in men, and it is always well to remember that, in a marked case of secondary syphilis, a medical man need have no doubt as to the correctness of his diagnosis because he has failed to discover the original sore.

Besnier says that in from 3 to 5 per cent. of cases of acquired syphilis in adults it is impossible to find any trace of a chancre. In cases of acquired syphilis in early infancy it is, perhaps more often than not, impossible to discover any evidence of the initial lesion. At a recent meeting of the Société de Dermatologie et de Syphiligraphie in Paris, Danlos quoted a case of a woman with multiple chancres of the breast, which had been communicated to her by a strange nursling. Shortly after the death of this infant, the woman suckled her own child, who a few weeks later developed general syphilis. The mother, believing that a chancre must inevitably appear, had watched her infant most carefully from day to day, but the point of entrance of the virus could never be determined. At the same meeting another case was quoted, in which the chancre completely cleared up in twenty-eight hours, though the adenitis persisted.

The primary lesion is neither an ulcer nor an erosion, but a new growth, a granuloma. The cutaneous lesions of syphilis belong, with those of leprosy, tuberculosis, glanders, &c., to the class named by Virchow ‘ the infective granulomata ’.

The disease first shows itself in the form of a papule, though it is but rarely seen in this early stage, particularly in women, and, even if observed, syphilis could not be diagnosed from such a papule with any certainty.

Although the initial lesion is neither an erosion nor an ulcer, the sore, when first seen, particularly in women, will, owing to secondary infective changes, almost invariably be found to be either an erosion, an ulceration, or a more or less funnel-shaped sore with thickened rounded edges sloping down to a smooth dry floor of a glistening, somewhat varnished appearance—the typical Hunterian chancre; or else the floor may be covered with a thin grey pellicle, which on removal exposes minute bleeding points. Again, if ulceration has not subsided, it may present a number of small pits, described by the French as ‘ vermoulu ’, or worm-eaten. In other cases it may be found as a dry papule, or a mass of induration, which gives the sensation that it might be readily shelled out—in fact it feels like a small hard elastic foreign body which has been let into the tissues. These last two types of sore, showing no evidence of ulceration, occur much less frequently in women than in men.

As already stated, the primary lesion may be ephemeral. It may become indurated again with the onset of secondary symptoms. It may be single or multiple, simple or mixed, phagedaenic or relapsing. (See Plate XLIX.)

It may be genital or extra-genital; the former, being of more frequent occurrence, will be first described.

But it must be remembered that whatever type the initial lesion may assume, be it apparently benign, or be it malignant, it is merely an indication of the virulence of the poison and of the powers of resistance to it of the bearer at the time of inoculation, and we are quite unable to draw any conclusions from it as to the probable course of any subsequent symptoms.

Genital chancres in women vary in the course of their development with the type and habits of the individual, and also with the situation of the sore. In the temperate, spare, dark-haired, otherwise healthy woman, who is in the habit of keeping herself dry and clean, there is a greater likelihood of the initial lesion not being discoverable, or, if found, of its being a typical single indurated sore.

On the other hand, in the case of stout women, who perspire freely, or have had their vitality lowered by such debilitating influences as insufficient food, alcohol, tuberculosis, gonorrhoea or other chronic vulvo-vaginal discharges, sepsis, or the state of pregnancy, the difficulty in arriving at a diagnosis as regards the initial lesion is greatly increased owing to the presence of vegetations, condylomata, &c.

It is often most difficult to decide the question of the diagnosis of syphilis from the initial lesion alone. Indeed in very many cases it is far better to delay and wait for the onset of secondary symptoms before giving a definite opinion.

The chief points to be considered in arriving at a diagnosis are the period of incubation, the induration of the sore, and the implication of the glands.

Incubation period. The period of incubation is perhaps the most difficult to determine. Experimentally it has been found to be an interval of twenty-three to twenty-seven days. But in practice, while the average duration is, perhaps, twenty or thirty days, it may be as short as ten days or as long as forty-five or more. A history of a shorter or longer period than these should only be accepted after the most searching inquiries. It has been noted that the incubation is prolonged in proportion to the age of the patient over 40 years of age. Sir Alfred Cooper thought that, if the infection be derived from a primary sore, the period of incubation would be found to be shorter than when a secondary lesion is the origin of the trouble.

Induration. In not a few cases it is impossible to recognize the presence of induration. It is greatly influenced by the situation of the sore, and Ricord taught that it was most marked where the lymphatics were most numerous. But in the case of a typical chancre the induration is, as the French say, 'à froid', that is to say, it occurs without inflammation. It may be evident in one of the three following varieties :—

1. The parchment-like variety—a thin layer of induration exactly underlying the sore. This may readily escape detection unless a careful examination be made by pinching up the ulcer between the finger and thumb. A peculiarity of this type is that it disappears sooner than the other varieties ; so that it may be absent when the patient is first examined, but may suddenly reappear with the onset of constitutional symptoms. This type of induration will be more commonly found when the sore is situated on a mucous surface.

2. The firm resistant induration of the typical Hunterian chancre was first named by Benjamin Bell 'the split pea variety'. It is but an exaggerated condition of the parchment variety, and, like it, does not trespass beyond the bounds of the original ulcer, which now, somewhat contracted, may be seen at the bottom of a more or less saucer-shaped depression. It is, as might be expected, much more persistent than the parchment variety. It is freely movable on the underlying parts, and gives rise to little if any discomfort. Indeed, it not infrequently happens that we are called upon to treat a patient with well-marked secondary symptoms who stoutly denies that she has ever had a sore. Yet examination shows an indurated chancre, of the presence of which the patient is quite unconscious.

3. Indurated oedema is a third variety, which is much more fre-

quently seen in women than in men. It far exceeds the bounds of the original lesion. It affects especially the labia majora, bearing out Ricord's observation that induration is most marked where the lymphatics are most numerous; this will be again alluded to in considering the chancres found on these parts.

Induration of the lymphatic glands is by far the most important of the three factors in the diagnosis of syphilis, as until this occurs it is impossible to arrive at any definite conclusion about the nature of the sore.

It is almost invariably present and is a much more constant phenomenon than the induration of the chancre. So constantly is this the rule that, as Ricord said, 'Adenitis follows the chancre as the shadow the body'; and later, Fournier was able in only 3 cases out of 267, a trifle more than one per cent., to satisfy himself that adenitis had never been present.

Induration of the lymphatic glands may appear to precede the induration of the primary lesion when the sore is on the genital mucous membrane and the induration, of the parchment type, has cleared up before the patient has come under observation. In other cases the sore may have again become indurated, and this may not take place until the secondary symptoms supervene.

But it must be remembered that in many women, owing to the large amount of adipose tissue of the parts, it is not always an easy matter to feel the enlarged glands. The glands implicated are those in anatomical relation to the sore, and as genital chancres are far more common than extra-genital sores, the inguinal glands are the most commonly affected. Owing to the free anastomoses of the lymphatic vessels it occasionally happens that the glands involved will be found on the side of the body opposite to that of the primary lesion. The enlargement of the glands is very persistent and may last for several months after the chancre has disappeared, which fact may form an important confirmation of the original diagnosis. This, perhaps, more especially applies to extra-genital chancres, and particularly to those cases of syphilis acquired in early infancy in which the chancre disappears very early. Induration of the glands begins about one week after the appearance of the sore: a single gland is first involved, this is followed shortly afterwards by those in its immediate neighbourhood, forming a more or less large group, among which the gland first invaded stands out prominently and is usually larger than the others.

In tubercular subjects the glands are often very prominent. In an uncomplicated case the individual glands are indolent, smooth, hard, elastic, painless, and discrete. The integument is not involved, but is freely movable over them. They have been likened to marbles, bullets, almonds, &c., and in former days these groups were known as ‘ the Pleiades of Ricord ’. As a rule, the only discomfort experienced is from the mechanical interference with movements caused by the abnormal swelling in these parts.

In spite of the fact that mixed infection is much more frequently observed in women than in men, one cannot help being impressed by the rarity with which the inguinal glands suppurate in women.

While the chancre may appear at any point on the surface of the genitalia, experience shows us that certain parts are more favourable than others for the virus to be implanted upon. The order of frequency with which the different parts are implicated will be found, as Fournier has shown, to be—the labia majora, the nymphae, the fourchette, the cervix uteri, the region of the clitoris, and last of all—the vagina.

The initial sclerosis of the labia majora may appear as an erosion, an ulcer, a papule, or a typical Hunterian chancre. It may vary according to its situation, whether on the internal surface, free margin, or external aspect. Or again, according to the type of woman, spare and thin as opposed to stout ; according to the health of the patient and her habits as to cleanliness, &c. ; as well as the presence or absence of such complications as gonorrhoea, soft sores, pregnancy, &c.

The sore will appear as a small oval erosion or ulcer with well-defined margins, with a clean, glistening base, often of a bright vinous red colour, when it is situated on the internal aspect of the labium in a spare woman who is cleanly and otherwise healthy. By carefully raising it between the finger and thumb from the deeper structures it may be possible to make out the parchment induration. But what is more usually found is that this little well-defined ulcer is situated on the inner surface of a large swollen and indurated labium. This *indurated oedematous condition* is but rarely seen in men, in whom it affects chiefly the scrotum, but it is a very usual type for the initial lesion to assume in women. When both labia are implicated, it is often quite impossible to determine the point of entrance of the virus. Probably in such a case the original lesion was situated in the neighbourhood of the fourchette, and some authorities think that the condition starts in a small suppurative mixed infection. Be this as it may, the thick leathery consistency of the labia is peculiar to, and in my opinion almost pathognomonic of syphilis. It is quite distinct from the boggy oedema arising from a purely inflammatory septic condition.

The initial lesion may be *multiple*; this condition, though far from rare in men, is an *extremely common one in women.* The two cases are quite analogous, and are due to a number of points being inoculated at the time of infection or very shortly after it. When the extreme delicacy of the integument of these parts is recalled, we can appreciate how readily small abrasions may arise during intercourse, thus forming numerous portals for the entry of the virus. The wonder is rather that we ever find a single lesion. The term 'satellite' sores, so often applied to early secondary lesions of these parts, is to be condemned as a misnomer, because they are entirely of a later development.

Multiple chancres of the labia majora are not infrequently seen as two juxtaposed indurated sores on the internal and apposed surfaces of the labia, a condition occurring fairly often in the male, where we find an indurated chancre at the base of the glans near the corona, and a second one on the immediately adjacent part of the prepuce. But the prepuce is not infected from the glans, nor is one labium from the other; this is shown by the one chancre appearing either at the same time or very shortly after the other. If one labium were infected from the other, we should find an incubation period of ten days or more between the appearance of the two sores. (See Plate L.)

Multiple Indurated Chancres. (See Plate LI.)

Case 2. ——, aged 27, height 5 ft. 0¼ in., weight 7 st. 10 lb. Condition on admission: there was a chancre behind the anus, a second partially surrounded the orifice, a third and fourth were situated one on each labium majus, while a fifth involved the base of the clitoris. These were all typically indurated. The glands in the inguinal regions were enlarged, prominent, and hard. There were mucous plaques on the tonsils; no eruption on the body could be demonstrated, but there was a marked collar of pigmentation on the skin of the neck.

Case 3. ——, aged 17, height 5 ft. 5 in., weight 9 st. 5 lb. Condition on admission: patient said that she had been ill for fourteen days. There was indurated oedema of the labia majora and minora, an indurated chancre on the outer side of the right labium minus, another on the posterior part of the right labium majus, and a third on the clitoris. There was considerable vaginitis. The inguinal and cervical glands were enlarged and hard. There was a general papular eruption on the trunk and neck. In the latter situation, two weeks later, the patient developed a well-marked pigmentary syphilide.

Case 4. ——, single, aged 21, height 4 ft. 10 in., weight 6 st. 1 lb. Condition on admission: the outer surfaces of the labia majora were covered with condylomata, and on one labium minus were two almost symmetrical chancres; these were flat, not particularly excavated, but they had sharply-defined margins. The floor was smooth, shining, and of a somewhat red vinous colour. The base or area of induration was of the parchment-like variety and was localised entirely to the area of the sores. The inguinal glands were enlarged and there was a pigmentary syphilide of the neck.

The *papular variety* is another form in which the initial lesion is seen. This is almost always multiple in women, the single indurated papule so common in men being much more rarely met with. When present it will be found to be indurated, somewhat rounded, raised above the general surface, more or less scaly, which renders it only slightly pinker than the tissues on which it rests. When multiple, this variety affects the labia majora, the nymphae, and prepuce of the clitoris, when these protrude beyond the vulva.

These papules occur either scattered over the surface or as a row of discrete and slightly scaling papules, of a greyish colour, along the free margin of the labium. Each is distinctly indurated, and the general lymphatic network of the part is not implicated. The initial lesion sometimes takes the form of a nodular cord lying along the free margins of the labia, the nodular appearance indicating the valves in the lymphatic vessels.

Case 5. ——, height 5 ft. 2½ in., weight 7 st. 5 lb. The patient stated that she had always enjoyed good health until three months ago, and for the eight weeks previous to admission she had been treated with medicine.

Condition on admission: there was a row of indurated papules along the free margins of the labia majora, which were not enlarged. The glands in the inguinal, right posterior cervical and left epicondylar regions were typically enlarged. There was a slight eruption on the abdomen, and rhagades between the toes. There was marked alopecia, and for a few weeks previous to entering the hospital the patient had been losing flesh. So far as she knew there had been no eruption on the scalp or neck ; but in the latter situation there was a well-defined pigmentary syphilide.

Case 6. ——, aged 5 years, was admitted into the hospital with a long, dry, nodular and indurated sore extending along the free margin of each labium majus. The inguinal and post-cervical glands were enlarged. There was a general pigmentary syphilide of the skin of the abdomen, and a more slightly marked one in the cervical region. In the mouth there was a mucous patch on the soft palate. The tongue showed on its dorsal aspect and near the free margin a very prominent, raised, almost warty ridge of condylomatous growths. The little girl, a foreigner, spoke no English, and the only history to be obtained was that the father had syphilis twelve years ago ; that he, his wife, and sister-in-law, who lived in the same house, had been treated for many years past for syphilis. Patient's brother, from whom she probably acquired it, was suffering from hereditary syphilis, though she herself showed no evidence of inherited disease. If this be a case of acquired syphilis, it is one of most unusual interest. The parents were both old syphilitics, the brother, from whom the patient is supposed to have acquired the disease, was only a few years her senior, and was, I am told, undoubtedly a congenital syphilitic.

A *single typical Hunterian chancre*, with a smooth callous base and thick rounded margins, is occasionally seen in patients who keep themselves dry and clean.

Case 7. ——, aged 23. Three weeks before admission the patient had had a vaginal discharge, which had cleared up before she entered the hospital. She noticed a sore on the vulva fourteen days after the onset of the vaginitis. This, on admission, was found to be a typically indurated chancre of the left labium majus, three-fourths of an inch in diameter; the thickened, hard, and rounded edges sloped down to a dry, varnished-looking base. The general structure of the labium was not implicated, in fact the chancre seemed to be attached almost by a pedicle, and might readily have been removed with a pair of scissors. It felt exactly like a small foreign body which had been let into the tissues. The inguinal glands were involved, and a week later she had a roseolous eruption on the neck.

The *relapse of the chancre*, if we except the early reinduration of the initial lesion, not infrequently seen at the onset of secondary symptoms, is apparently of much rarer occurrence in women than in men, possibly because our attention is not called to the condition. Within the last few months I have had two cases in the Lock Hospital of this condition.

Case 8. ——, single, aged 20, admitted February 20, 1907. On admission there was an indurated chancre on the right labium majus, together with superficial ulcerations on the internal aspects of the labia minora, with profuse vaginal and cervical discharge. The glands in the inguinal and posterior cervical regions were enlarged and hard. The fauces were inflamed and mucous patches were present on both tonsils. There was a general roseolous rash over the body, and a slight pigmentary syphilide of the neck.

In April the tonsils were severely ulcerated. In July the throat was still troublesome. On August 10, without any discoverable cause, the patient informed me that the original sore had returned. It occupied exactly the site of the original lesion, near the posterior part of the right labium majus. It was about a third of an inch in diameter; its margin, raised, hard, and rounded, sloped down to a dry, shining, indurated base. At the same time the glands in the right groin again became indurated. The treatment now was an iodide mixture and calomel fumigations, and by August 27 the sore had almost entirely disappeared.

During the interval, February 20 to September 14, the patient's general condition had very much improved; she had increased in weight from 10 st. 2 lb. to 11 st. 6 lb.

Case 9. ——, aged 26, single, admitted June 8, 1906. Condition on admission: there was an indurated chancre of the left labium majus with indurated glands in the left groin, a vaginal discharge, a macular eruption over the trunk and extremities, and a severely ulcerated left tonsil. She was treated with calomel injections, but on July 2 the pain which they caused interfered so much with sleep that the treatment was changed to pills of mercury. On July 30 the sore again became indurated, though her general condition had much improved, and she had gained 12 lb. in weight since admission. During the next twelve months she progressed fairly satisfactorily, but was always very susceptible to mercury, which could only be given with great caution. On June 8, 1906, she weighed 8 st. 11 lb. (8 st. 4 lb. on admission), but at Christmas, 1906, she weighed 9 st. 13 lb. By September 14, 1907, she had gained 9 lb. On August 14 the sore on the left labium majus and the glands in the left inguinal region were again indurated. On September 2 the notes say that the sore on the vulva was rapidly healing.

These *relapsing indurations* may be met with at any time after the disease is acquired; they may even occur repeatedly. I know of one male case in which the chancre relapsed five times in the first thirteen months after infection, during which time the patient was continuously under treatment, but was leading an irregular life, and having intercourse frequently.

When they recur thus early in the complaint they exactly resemble in position and in general appearance the original lesion, and appear to have no effect on the course of the disease. They may recur without any obvious cause; but in the cases in which the recurrence follows intercourse the incubation period is a very short one. In an account of eighteen cases of indurated pseudo-chancres I published in the 'Lancet', 1896 (May 30, p. 1479), six of them occurred after intercourse at the following intervals: one immediately, one within four days, two within a week, the remaining two on the ninth and tenth days respectively.

In the majority of these cases the stress of the early symptoms will be found to have fallen especially on the mucous membranes, the mouth, throat, &c., in preference to the skin. In 1783 John Hunter said, 'It often happens that after chancres are healed, and all the virus is gone, the cicatrices ulcerate again, and break out in the form of chancres. They appear to be a consequence of a venereal complaint having been there, as they seldom attack those who never had gonorrhoea or chancres.' In the 'Archives Générales de Medicine,' 1862, Diday published twenty-five cases of second attacks of syphilis, twenty of which he himself had seen. In fourteen of these the only evidence of re-infection was the indurated chancre.

These lesions at times disappear spontaneously, and without being influenced by treatment. In the paper in the 'Lancet' (1896, May 30, p. 1479), from which I have quoted freely, I suggested that an explanation of these lesions might be found by combining the theory propounded by the late Sir James Paget on relapsing inflammations with the explanation of indurated pseudo-chancres offered by Prof. Fournier, viz. that we should consider these pseudo-chancres as due to the disturbed or interrupted nutrition of the new materials that were formed among the tissues deteriorated in the previous inflammation; and that they owe their peculiar likeness to the infecting sore because they had their origin and cause in the primary infection, and are now absolutely independent of all further contagion.

I ended the paper with Mr. Hutchinson's most important warning: 'The knowledge of the facts as to recurring chancres is of very great importance, since without it very serious mistakes may occur, not only as regards treatment, but in reference to social and medico-legal questions.'

The Mixed Sore. Strictly speaking, almost every sore in women belongs at some time or other, in the course of its evolution, to the mixed type, and it is only in the case of the woman who keeps herself scrupulously dry and clean that we may hope to find the dry papule or Hunterian chancre which has never ulcerated.

But by the term 'mixed sore' is generally understood a syphilitic chancre contaminated by the presence of septic material, or a sore the result of a double infection, by pyogenic organisms and syphilis. In such sores in recent times the presence both of the strepto-bacillus of Ducrey, which he regarded as characteristic of soft sores, and the *Spirochaete pallida* have been demonstrated.

The soft sore, or ulcus molle, is, more frequently than not, a multiple lesion, and each individual sore forms a most convenient point of entry for the specific agent ; and so, in cases of mixed infection we generally find more than one primary lesion. If the case be seen sufficiently early, and appropriate treatment be resorted to, these soft sores may be healed, and nothing apparently left behind. But in the course of time, i.e. at the end of the incubation stage, each point thus inoculated will become the seat of a primary lesion; or these soft sores may not be thus early treated, but may be still present when the patient comes before us with undoubted secondary lesions ; in such a case it may be often very difficult to determine the presence of induration, which seems to have been dissolved away by the septic infection, as soon as it is formed. However, by clearing away the products of inflammation, it may be possible, by careful examination, to make out a parchment-like layer of induration at the base of the sore or sores. This observation also applies to the case of a chancre infected secondarily by pyogenic organisms, either from a soft sore, or gonorrheal or other vulvo-vaginal discharge. In such cases of mixed infection, where it is almost, if not quite, impossible to determine the presence of induration, the secondary symptoms will often be found to be of a severe type. It would appear as though the solution or melting away of the induration by the septic infection, permitted a more rapid and general dissemination of the specific agent throughout the tissues.

Chancre of the Cervix Uteri.

This is generally thought to be a rare lesion. It is certainly the least known and the most frequently undiscovered of all genital chancres that occur in women. Fournier noted its occurrence in thirteen cases out of 249.

It should be sought for in all cases where there is the least cause for suspicion. It must be looked for *early*, as by the time that secondary symptoms have appeared all traces of its presence may have cleared up.

CASE 10. ——, aged 21, single. Admitted August 19, 1907, with a history of a vaginal discharge for the past three weeks. The left labium minus was oedematous and the inguinal glands were slightly enlarged. On the anterior lip of the os uteri was a rounded, smooth, very slightly convex, dark, purple-red chancre, which bled readily and looked like an enlarged papule. By September 2, the chancre was undergoing resolution; it had lost its deep purple tint; it was of a lighter and brighter red, and was flattening. There was a very faint rash on the thighs.

The chancre, more usually single than multiple, is rounded, smooth, glossy, and more often convex than concave. Its limits are more or less clearly defined, according to the state of evolution at which it has arrived. Its edges are but ill-defined, in fact, there are usually no edges, correctly speaking. It either fades into the neighbouring tissues when it is flat, or it joins with them in a slight declivity when it is somewhat raised. It bleeds readily when touched by the speculum.

When seen early, Fournier says, 'this lesion shows a colour of a waxy grey (gris lardacé), recalling the colour of spots of scirrhus, apparently due to a sort of pseudo-membranous coating. This colour may turn to a grey-white, a dead white, or a yellowish-white enamelled with ecchymotic spots.' At the end of a very short time—three or four days—he says the change is absolute and it recalls the appearance of an enlarged reddish papule.

It gives rise to little or no discomfort; the patient may be totally unaware of its presence. It has this characteristic, that it may disappear more rapidly than any other chancre.

So speedily do these changes in evolution follow each other, so rapid is the healing, that if the chancre be not sought for previous to the onset of secondary symptoms all traces of it may have disappeared. This rapid healing and absolute disappearance of the chancre are due (1) to its situation, which ensures for it freedom from friction and irritation, to which chancres on other parts are exposed, and by which their longer duration is maintained; (2) to a relatively raised and even temperature; (3) to an equable state of moisture, by which the surface of the chancre is being constantly macerated.

So rapid, indeed, is this process of healing that Thibierge asks whether many cases of so-called conceptional syphilis are not cases of syphilis arising from an unrecognized chancre of the cervix uteri?

The two cardinal signs of a chancre are difficult to determine in the case of this lesion, viz.: (1) induration; (2) the enlargement of the nearest lymphatic glands.

Induration. Unless one has a case like the classical one of Ricord, where the chancre occurred on the cervix of a prolapsed uterus, digital palpation is highly dangerous, and neither necessary nor justifiable. Its presence may be detected by means of a long pair of dressing forceps, and the presence of a very regular and distinct induration all around the chancre may thus be made out.

Adenitis. The lymphatics of the cervix are connected with the glands of the pelvis, and only seldom give rise to a mass which can be appreciated.

Occasionally, however, in spite of its special connexions, a chancre of the cervix uteri may implicate the inguinal glands, a fact to which, as Thibierge says, but little attention has been drawn; and yet, he continues, this is no more paradoxical than the development of a bilateral inguinal adenitis following a chancre of the nymphae. Most observers attribute this to the richness of anastomoses of the lymphatics of the two sides, but it seems more rational to admit that it is due to a rapid diffusion of the poison into the tissues in the neighbourhood of the chancre, a diffusion which brings it into the territories of other lymphatic glands.

Chancre of the cervix uteri may ulcerate, at times severely, and the diagnosis may then be very difficult to determine. At the same time one must be careful not to take for a syphilitic sore an ulceration from any other cause; this also may perhaps be indurated. In such a case the induration is less regular, following the different points of the surface irregularly. This, perhaps, especially applies to a malignant ulcer. The lesion may be multiple and of considerable extent over the vaginal aspect of the cervix and resemble a soft sore; the base of the ulcer may be irregular and budding, dotted over, perhaps, with patches of a yellowish brown, pseudo-gangrenous, slightly adherent coating, the removal of which exposes extremely painful ulcerated spots. These do not necessarily bleed readily, but the tenderness may be so great as to seriously interfere with the use of a Playfair's probe or dressing forceps to determine the presence of induration. As a rule, however, with due care and delicacy, a ring of induration may be made out surrounding the ulcer. At the same time, it must be remembered that in many of these cases we are not able to reach the implicated pelvic glands and the inguinal glands are not involved. Under these circumstances, Thibierge has suggested trying the effects of auto-inoculation of the abdominal wall with some of the sero-purulent matter from the ulceration. Failure of the experiment may be accepted as strong presumptive evidence in favour of such a lesion of the cervix being syphilitic.

Chancre of the cervix uteri must be diagnosed from a 'simple' (so-called) erosion of the cervix; this lesion, a not uncommon one, shows as a slightly depressed area, reddish in colour, and extending generally from inside the os externum; such a lesion is very chronic but is not indurated.

From Epithelioma. This condition, though rare, is not unknown in women between twenty and thirty, though it is much more frequent between forty and fifty. It is most frequently met with in those women who have had large families: not quite two per cent. of all cases occurring in the absolutely sterile. The form of malignant ulcer most likely to be confounded with syphilis is the so-called conical ulcer, bounded by a hard ring of infiltrated tissues. The points to be noticed are the age of the patient; whether she be a multipara or nullipara; the wasting, which in some cases is a marked and early symptom; the occurrence of haemorrhage at other than the times of the menstrual period; the character of the secretion, which in a case of malignant ulceration is thin and exceedingly offensive; pain, this being quite a late symptom; and lastly, the fixation of the cervix by the spreading growth.

It has been observed that a chancre of the cervix of a pregnant uterus has a much longer duration than the chancre of this part uncomplicated by such a condition. And further, that the induration, which accompanies it, may give rise to such an amount of rigidity of the os as seriously to interfere with parturition, so that if a chancre of the cervix be recognized in a pregnant woman, very active treatment should be straightway adopted in order to clear up the chancre as thoroughly and as early as possible.

Case 11. ——, single, aged 26, was admitted into the Hospital with two primary lesions of the cervix uteri looking like large, dully red, oval, convex papules, one on each lip of the cervix, partly surrounding the external os. The inguinal glands were hard and discrete: there was a fading roseola distributed generally over the body, and a large gummatous looking ulceration over the upper part of the right tibia. The sores were first diagnosed eighteen weeks before admission and she had been treated all the time. Fourteen weeks before entering the Hospital, she was delivered of a premature eight-month child, who only lived three days. The rash had been out and had disappeared before the confinement, but now broke out afresh.

Successive Chancres. In the last few years attention has been drawn, chiefly perhaps, by the French authorities, to cases of multiple chancres, in which the lesions appear at considerable intervals of time from each other. The possibility of this is denied by many authorities, who contend that by the time a chancre can be recognized as such, the whole system is syphilized and immune against the production of a fresh primary lesion, and that the recorded cases are due to errors of observation on the part of the patient, the doctor, or both. Some time ago I saw a case of a digital chancre which appeared nine days after the appearance of a chancre on the penis. Remembering the difficulties met with in cases of digital chancres, the often long incubation period, &c., this might possibly be considered a case in which observation was at fault. But within the last few weeks I have seen a man with a typical hard chancre on the left half of the prepuce, a second about the middle of the right lateral aspect of the sheath of the penis, and a third in the right peno-scrotal fold; each sore was a typical indurated chancre, measuring about three-quarters of an inch across. The patient assured me that the second sore had appeared quite two days after the first, and the third the same interval after the second. Any one of the three lesions might have been accepted as a typical example of the primary Hunterian chancre. In such an organ as the penis one would certainly not have expected to meet with such a condition, if we are bound by the theory that the marked induration of a syphilitic chancre is indicative of the fact that the system is now immune against the appearance of further chancres. But our previous conceptions of syphilis are, perhaps more so than in any other disease, being constantly modified. In 1905 Queyrat in Paris succeeded in producing successive chancres in three cases by auto-inoculation. In the first two, the original chancres were five days old, and in the third, six days. I cannot recall quite analogous cases in women to those above mentioned, unless we are to consider as such the rather rare lesion of juxtaposed sores of the labia majora. R. W. Taylor says: ‘In women genital chancres may give rise at a later time to lesions of the opposite side of the genitals or of the thighs. In these the syphilitic secretion, which escapes and bathes the neighbouring parts, acts as an irritant and develops new chancres.’

Years ago, when the question, raised by Boeck, of syphilization was being investigated, both Taylor and Bumstead observed the occurrence of these successive lesions, especially in the second period of incubation. Much was hoped for from this method of treatment, but they (Taylor and Bumstead) ‘incontinently failed in ameliorating, abating, or curing syphilis by syphilization’.

CHAPTER XIX

EXTRA-GENITAL PRIMARY LESIONS

Extra-Genital Chancres. The virus of syphilis may be implanted on any point of the surface of the body, and if the inoculation be successful, it will be followed by the formation of a chancre, with implication of the set of glands into which the lymphatics from the affected part drain.

In 1893, Vignolo Lutati said in the Italian 'Journal of Dermatology and Syphilis' that in 509 cases of primary syphilis in women, he had only met with thirty examples of extra-genital chancres. These were distributed as follows: Ten on the nipple, two on the areola and breast respectively, eight on the upper lip, one at the labial commissure, four on the tongue, two on the cheek, and one on the chin. These lesions are more frequently found in women than in men, and are thought to be commoner in the aged than in adults.

Such a chancre may be acquired venereally, e.g. by perversion of the sexual act, or accidentally and innocently, by some small wound or abrasion becoming infected with the syphilitic virus. When situated on the general surface of the body, such chancres, unless irritated, are not prone to ulcerate, but are dry, chronic, and callous sores. The facility with which the presence of induration may be determined will depend upon the position the sore occupies, and the amount of fatty tissue present: i.e. a difficulty is often found in isolating such sores from the underlying tissues, and here, as with genital chancres, very great assistance in arriving at a diagnosis is found in the condition of the anatomically related lymph-glands. It must be remembered that many of these cases being accidentally acquired and without the slightest suspicion as regards their true nature, are treated as simple sores.

Van Buren and Keyes (1877) quote the following most instructive case. A girl aged 16, who denied having had sexual intercourse, and on examination was found to be a virgin, was admitted with general syphilitic roseola and sore throat. It was impossible to discover any ulceration on any part of the body, the only evidence of a primary lesion was a small cicatrix of purplish colour and slightly hard, upon the radial side of the right fore-arm. The girl apparently was not aware of its presence. The girl was a nurse and had been carrying a baby, often without a napkin, on her bare right arm. Examination of the baby showed the anus surrounded with mucous patches. Bumstead quotes Rollet's case of a lady, who acquired a labial chancre from her cook, this person having numerous mucous plaques in the mouth. Both mistress and servant were in the habit of tasting, out of the same spoon, the dishes prepared for the table. Only a few weeks ago I saw a gentleman who gave the following history. About twenty years ago he slipped in the street and grazed the back of his hand. A bystander, anxious to render 'first aid', applied to the bleeding wound a piece of sticking plaster, which he had previously moistened with his own saliva. My patient thought nothing further about it till some three or four weeks later when a chancre developed at the site of the injury, followed later by the usual constitutional symptoms. In a recent number of the 'Annales de Dermatologie et de Syphiligraphie' an almost analogous case was given; the actors in the tragedy, for tragedies such cases are, being a small child and a strange lady.

From one's own experience and from our medical literature very many examples might be given showing how readily and yet how innocently the disease may be acquired.

As with genital chancres, those at present under discussion may be single or multiple; the type of chancre will vary with its situation, the amount of irritation it is exposed to, and the condition of health of its bearer.

Chancres of the General Integument. A few years ago, a man, who was attending among my out-patients for syphilis, brought his wife and eight-weeks-old infant to see me. On examining the child, a well-nourished girl baby, I found an indurated chancre in the fold of the left groin, together with a general roseola over the chest and abdomen. The mother had many condylomata about the vulva, a general papulo-squamous syphilide and severely ulcerated sore throat: she had been infected by her husband a few weeks before the birth of the child. The case was one of breech presentation, and the accoucheur had been obliged to use an instrument to bring down a leg, and in passing it had evidently inoculated the fold of the groin from the vulval condylomata of the mother.

The upper and inner aspect of the thigh is a not uncommon place to find a chancre in women. It may have its origin in an accidental abrasion during attempts at coition, or will, I believe, more commonly be found in those women, who either fear the risk of pregnancy, and so will not allow proper intercourse, or who believe, as so many men and women do even in the present day, that syphilis can only be acquired in the ordinary sexual act. We occasionally learn from a woman that her late partner had positively assured her of the impossibility of thus acquiring the disease.

Such a sore starts as a small 'pimple', gradually increasing in size till it may be as large as an inch or even more in diameter. It is generally single, flat, often scarcely raised above the integument on which it is placed, with a dry shining base; though this latter condition will depend upon the habits of cleanliness observed by the patient. Owing to its situation it is often difficult to raise it off the deeper structures in order to make out the induration, and generally the glands first implicated will be those below Poupart's ligament.

Chancre of the Abdominal Wall. A few weeks ago I saw a case of a sore situated in the central line midway between the symphysis pubis and the umbilicus. The date of infection was impossible to determine, but I was told it had first appeared as a small, dark, red lump, which the patient, under the impression that it was of the nature of a boil, had pricked and squeezed. Proper precautions as regards the cleanliness of the needle had apparently not been taken. For, when I saw the lesion first, it was of the nature of a discharging inflamed sore, measuring half an inch across. The glands in each groin were enlarged and hard, as was also the sore (this latter possibly the result of the squeezing to which it had been subjected). At the end of a week, under simple treatment, the inflammatory condition was clearing up. The base of the ulcer was cleaner, drier, and more glazed; the edges raised, thickened, and indurated. Three weeks later all doubt as to the diagnosis was cleared away by the appearance of a general papulo-squamous eruption, and specific treatment was promptly instituted.

Chancre of the Anus and Rectum. This may arise from accidental contact with the male organ during intercourse, or the poison may be carried there by vaginal discharges, or by the use of infected instruments, such as enema syringes, &c.

If situated just within the orifice it may appear as an erosion or ulcerating surface. Induration is not marked, and, as a rule, it gives rise to very little discomfort.

The glands implicated will be those situated at the inner end of the chain along Poupart's ligament, the lymphatics of the anus passing round the inner surface of the thigh. In a well-marked case of syphilis, in which the original lesion cannot be discovered, with typical glands at the outer end of Poupart's ligament, the possibility of the chancre being intra-anal should always be remembered.

Some few years ago I saw a woman about forty years of age who was admitted into the hospital with a large ulcerating surface on the wall of the lower end of the rectum, followed later by constitutional symptoms; in this case the pain in defaecation was excruciating. The woman was married and had acquired the disease from her husband, who assured her that by having intercourse thus, she could not be infected. On several occasions I have come across illustrations of this peculiar superstition; private patients have assured me that they always believed that it was impossible to acquire syphilis by anal intercourse, until convinced to the contrary by the appearance of a chancre on the penis. The anal chancre must be diagnosed from anal fissure. This is crack-like, generally very painful, and does not implicate the glands. From a suppurating haemorrhoid, in which case there will generally be found to have been a previous attack of piles or bleeding, or from the ulceration sometimes seen to arise from infection by gonorrheal or other vulval discharges.

Chancre of the Lips. The lips and mouth, next to the genital organs, are probably the most common site of the initial lesion. This is just what one would expect, seeing what a peculiarly suitable and commonly infected medium for the growth of the specific agent the mucous lining of the oral cavity forms. It is delicate, constantly moist, of a somewhat raised and equable temperature, and is always being more or less irritated, by movement and the passage of food, drink, &c. And so we find it the seat of election of probably the most highly infective of all syphilitic lesions, the mucous plaque. The skin covering the red substance of the lip is thin and delicate, and particularly prone to cracks and fissures, fitting portals for the entrance of the virus.

Infection may be caused, directly by unnatural offences, suckling, kissing, &c., or indirectly through some infected object—feeding utensils, musical instruments, coins, &c., coming in contact with an abrasion on the lip.

Here, as elsewhere, the initial lesion may be so trivial and ephemeral as to disappear within a week, having been regarded as a crack or abrasion due perhaps to a cold ; and here too, the most important and perhaps the only evidence of the inoculation will be the well-marked and generally typical involvement of the glands in the submaxillary, sublingual, and posterior cervical regions. I have said ‘ generally typical ’, because, occasionally, these inflame, become matted together and suppurate, owing to the apparently trivial little abrasion having been infected by septic organisms of the mouth. In lip chancres, however, it is not unusual for the glandular implication to be so marked as to give rise to a considerable amount of obstruction both to deglutition and speaking. In such a case the incorrect diagnosis of mumps has before now been arrived at. The lesion is thought to be more common in women than in men, and to affect the lower in preference to the upper lip. But in the last three cases I have met with, in two the chancre was on the upper lip. These sores seldom become phagedaenic ; but Arthur Ward quotes a case of a dentist's assistant, who inoculated himself with a tooth-plate on the lower lip and chin and developed two typical chancres. The lip one, owing probably to oral infection, sloughed and resulted in very considerable deformity.

Owing, perhaps, to the fact that this lesion is often innocently acquired, and that no suspicion arises as to its true nature, one generally sees a case of lip chancre when the lesion is well marked. We get a history that it has been present for weeks, it may be months, and other confirmatory signs of the disease may be well marked on the body at the time of our interview with the patient. Extra-genital chancres often persist for a longer time than genital ones, probably because their true nature is unsuspected, and of these the labial chancre endures the longest. Another point of interest in connexion with labial chancres is the very early appearance of roseola, a point to which attention was first called, I believe, by MM. Gaucher and Milian, who in 1893 published eight cases of labial chancres, showing the early appearance of roseola. The shortest period after diagnosis of the chancre was fifteen days, and the longest twenty-eight—a marked shortening of the normal forty-five days. They think that the general invasion of the organism is more rapid by this road of infection than by others ; that the greater vascularity of the parts may explain this peculiarity, a double route for the virus, both by the vessels and the lymphatics, being supplied ; and, further, they argue that, in general syphilitic invasion, the poison makes itself more rapidly felt when it uses the vascular, in preference to the lymphatic route ; in the same way as a sarcoma, which spreading by the blood, becomes generalized much more speedily than an epithelioma which invades by way of the lymph channels. It will be remembered in Jullien's oft-quoted case of two medical men who accidentally inoculated themselves during an operation on a syphilitic patient, directly into the blood, that secondary symptoms without the previous formation of a chancre appeared thirty days after the accident, and nine days before the onset of the same symptoms in the patient.

Recently, Lèvy-Bing showed a case in Paris of a patient who had had a labial chancre for thirty days, and in whom he had determined the presence of roseola fifteen days previously.

When first seen, a labial chancre generally presents itself as an oval mass apparently in the red substance of the lip. Its surface, but slightly excavated, unless it has been irritated, is dry, smooth, and may have a varnished appearance, with no particular tendency to bleed; its borders are indistinct as they fuse with the surrounding induration, which is marked, more so perhaps than with any other chancre, if we except the indurated oedema already alluded to as affecting the labia majora. The lips are richly supplied with lymphatics, thus we find here another example bearing out Ricord's observation, that induration is best marked where the lymphatics are most numerous. The lip is pushed out prominently, and conspicuously disfigures the face. If the sore extends into the mouth, this part of it will generally be found to be ulcerated. The lesion may be found at any time from babyhood to old age. In early infancy, as we have already seen, chancres have a tendency to disappear quickly, and to leave no trace behind them. In the young and up to middle age the sore may have to be diagnosed from impetigo, which is generally multiple either here or on other parts, a suppurating ringworm, herpes, inflamed sore, &c. But here the early onset of roseola may be of great assistance in determining the true nature of the case. Again in later life this lesion has especially to be diagnosed from epithelioma. In this latter, the surface is more ragged and irregular, it bleeds readily, the edges are rolled over and thickened, and the glands are later in being involved. In this case the early onset of the roseola will not help us, for it has been noticed that in syphilis acquired in old age, the incubation periods both of the chancre and of the secondary symptoms may be much prolonged.

The two following cases will be found to illustrate many of the points alluded to in the above description of the labial chancre:—

Case 12. ——, aged 13, admitted for a chancre of the left half of the upper lip. Her mother, I was told, took babies in to nurse, and the source of the patient's trouble, a poor wizened, clay-coloured, loose-skinned, and undeveloped infant of a few weeks old became at the same time an inmate of the hospital. On admission the chancre had given rise to a considerable protrusion of the lip; it was about the size of a hazel-nut, indurated and feeling like an oval foreign body which had been let into the red surface of the lip near the outer margin. The edges were not particularly raised nor marked, the base was not excavated, but was dry, and with a somewhat varnished appearance. The submaxillary and posterior cervical glands were hard, smooth, and separable. The chancre had been diagnosed eight weeks previously, during which time she had been under treatment. In addition to the chancre, she had mucous plaques on the right labium majus and on the fauces, together with a general roseola of the trunk and limbs. This last, she stated, had appeared fifteen days after the diagnosis of the chancre. Seven weeks after admission, or fifteen weeks after the appearance of the chancre, which was still very evident, she developed a well-marked pigmentary syphilide of the neck. (Plate LII.)

Case 13. ——, aged 19, admitted with an indurated oval swelling of the left half of the upper lip; the sore had extended into the mouth, and this part was covered with a yellow-white slough. There was a general enlargement of the sublingual, submaxillary, posterior cervical, epitrochlear, and inguinal glands. She had a vaginitis; a very dry skin, which was covered with a roseolous and squamous eruption. According to her statement (and she was a difficult patient to extract a definite history from), the chancre had only been present two weeks.

Chancre of the Tongue. Of the primary lesions which have their site in or about the mouth, the lingual chancre occupies the second place, after labial chancres, in order of frequency.

Inoculation occurs in the same way as a lip chancre. It may be multiple, though more frequently the lesion is a single one. As commonly seen, it appears as a well-defined oval nodule with thickened rounded margins, which, with the base, are markedly indurated. The surface is more or less excavated or saucer-shaped, generally more so than in the case of the labial chancre; it is red and eroded, or may be covered with a grey pellicle, or present a somewhat glazed appearance. If a fissure of the tongue be inoculated, the chancre assumes the shape of the fissure, being lengthened rather than oval. These lesions give rise to but little discomfort, and the submaxillary and submental glands will be found to be typically involved after a short time. A lingual chancre may have to be diagnosed from secondary syphilitic affections of this part, e.g. a mucous plaque, in which perhaps a pseudo-induration has been produced by the application of silver nitrate or some other caustic; from papillary growths—these, however, generally occur in the centre of the dorsum of the organ, and are really a mass of hypertrophied papillae, whereas the surface of a chancre is devoid of papillae; from a tubercular ulceration, in which, as in the mucous plaque, a pseudo-induration may have been produced as the result of the treatment employed. Tubercular lesions are generally multiple, and we may find concomitant evidence of tubercle in other parts; at the same time it must be remembered that the two diseases may co-exist. From epithelioma—this may start as a nodular growth, and the same sets of glands may be early involved, though these latter, if the lesion be malignant, will generally be found to be more matted together than in syphilis. The age of the patient is another important point, as, if under forty, the chances of the lesion under discussion being syphilitic are much increased; and lastly, we have to bear in mind how seldom cancer affects either the lip or tongue in women.

In a doubtful case, the presence of the *Spirochaete pallida* might be sought for, always remembering that it requires considerable experience to demonstrate the organism, and that it is almost useless to look for it if mercurial treatment has been already commenced. Recourse may be had to the so-called intensive treatment of syphilis to clear up the diagnosis, and for this purpose, perhaps, intramuscular injections of calomel are the most suitable. So susceptible are syphilitic lesions of the tongue to this drug that Fournier has called the tongue the organ of calomel.

Chancre of the Tonsils. This lesion is probably not so rare as is generally supposed, being more frequently met with in the present day than formerly, owing probably to its being more systematically sought for. In every case of syphilis the throat should be carefully examined. Syphilis, as a rule, is a painless disease, and a patient will often assure one that there is nothing the matter with the throat; examination may, however, show that most extensive destruction of the soft parts is taking place, although the patient is quite unaware of the mischief. Never accept the patient's word that the throat is all right, but look for yourself. The lesion is commoner in women than in men, this probably being due to the disgusting practice of oral intercourse. In the often widely-open crypts, the specific agent is readily arrested; but the tissues in which the organ rests vary so much in different patients that it is impossible to define a typical lesion.

This lesion, Fournier says, ranks third among the syphilitic ulcers of the mouth; he recognized it in forty per cent. of his cases. The sore is generally single. It often covers the whole tonsillar surface, and may even extend to the pillars of the fauces and base of the tongue. The right tonsil is more frequently affected than the left. The erosive form is the most common and gives rise to but few symptoms—oedema, slight redness, and superficial ulceration. In the ulcerating form there is pain and dysphagia. It is a red-brown, grey, or yellow ulcer, with considerable induration of the whole tonsil. The anginal form, the least frequent, is a tonsillitis, with ulceration, pain, dysphagia, and general constitutional disturbance. A diphtheritic or gangrenous form is met with in some rare cases. The adenopathy, the persistence, as well as the unilateral character of the lesion, the time of appearance, and the course of the disease are all important aids to a correct diagnosis. A benign case may last five weeks.

The position of the tonsil corresponds externally to the angle of the jaw, and the lymphatics drain into the superior deep cervical glands. A matted, tender mass will be found therefore with these lesions above the centre of the sterno-mastoid muscle. The induration of these chancres is often very marked, but they are most difficult to palpate, and even then this is only done with considerable risk to the examiner, as the following case shows: A girl aged eighteen was brought to me with a chancre of the right tonsil. It occupied the whole organ, which was swollen, dark red, and glistening, ulcerated on the surface, which was covered with an adherent cream-coloured slough. It was not particularly painful, but the glands in the neck were tender.

Her soldier friend, from whom she had acquired it, had, I understand, sore places in the mouth. The doctor who brought her to me had recognized this lesion as a syphilitic chancre, and had examined for induration, with the result that he got an indurated chancre of the right index finger, and typical glands in the axilla, and later went through the usual course of an attack of syphilis.

The tonsillar chancre is almost always unilateral, an important point to be remembered, and one of great assistance in arriving at a correct opinion as to the nature of the sore. We may, however, be called to diagnose it from the unilateral crateriform tonsillar ulcer occasionally met with. This ulcer has a sloughing base, thickened edges, and slight adenitis. It may be distinguished from the chancre by the slight adenitis and the rapidity with which it yields to iodized applications and boric acid gargles, the tonsillar chancre being often very persistent.

Chancres of the Eyelids. This is not a rare lesion. Bulkley thinks it accounts for four per cent. of all cases of extra-genital chancres. It is met with at all ages: in the new-born, from accidental inoculation during parturition, up to old age, e.g. Berry's case of a woman over eighty, who developed a chancre of the eyelid from nursing a case of infantile syphilis. The virus is often carried to the lid by rubbing the part with an infected finger, which may account for the lesion being more common on the right than on the left side. Only last September I saw a typical chancre on a right lower lid, which had developed at the same time as an indurated sore on the penis, four weeks after infection. It may arise from a scratch by an infected person or from infected saliva reaching the part. Fournier records the case of a colleague who, when applying a caustic to some oral plaques, was infected by the patient spitting straight into his face. It may occur as the result of the practice, not unknown among the poorer classes, of removing a foreign body from the eye by licking: but perhaps the most common way in which infection is conveyed is by kissing on the eye. In many of these cases it will be found impossible to arrive at a diagnosis of syphilis previous to the onset of constitutional symptoms.

In a typical case the alteration in the physiognomy is as evident as in the case of a labial chancre ; the lid is protruded in a markedly characteristic manner, as though it were supporting a reddish foreign body inserted in its substance. Either one or both lids may be affected, and it is thought to be rather more common at the inner than at the outer canthus. It may extend on to the ocular conjunctiva. But, fortunately for the patient, as a rule the palpebral conjunctiva is alone implicated, and in such a case, if the condition be seen early and the patient be amenable to treatment, the prognosis is decidedly favourable. In many cases, however, the only discomfort experienced is the unsightly appearance such a lesion produces, it is thus very often neglected, and the patient perhaps does not come for treatment until adhesions have formed between the palpebral and ocular conjunctivae, or with the formation of an entropion or ectropion. The chancre generally starts as a papule or pimple, which ulcerates, becomes markedly indurated, giving rise to the characteristic pushing forward of the lid, the margins of the ulcer are clean cut, and the floor somewhat saucer-shaped with very often a scanty grey secretion ; or the entire lid may be implicated, swollen, and greatly indurated. In such cases it is impossible to make a diagnosis before the onset of secondary symptoms. The glands involved are the pre-auricular, the superior deep cervical set, and sometimes the submaxillary. The pre-auricular gland, when involved, is a sign of special diagnostic value. The lesion is a peculiarly persistent one.

A chancre of the eyelid has to be diagnosed from a vaccine pustule—which probably occurs accidentally and perhaps more frequently than is supposed, from a tubercular or malignant lesion, or a gumma. In the early stage the primary and the tertiary lesion have been mistaken the one for the other. At this period each consists of an ulcerated surface with sharply-cut edges and induration. In the chancre the discharge is, perhaps, the more copious, and the pre-auricular glands are enlarged. In the tertiary lesion there may be a history of a previous attack of syphilis, gummata elsewhere, together with keratitis punctata, syphilitic iritis, &c. The treatment, apart from general constitutional medication, consists of the local application to the sore of some mercurial preparation, such as the yellow oxide of mercury ointment, 4 gr. to the ounce. If, however, the case be more severe, with implication of the ocular conjunctiva and profuse discharge of pus, or in the case where the whole lid is involved, and if syphilis can be diagnosed, the patient should be brought as speedily as possible under the influence of mercury. This is best effected by the intensive method of intramuscular injections, which is, of course, additional to any local treatment.

Chancres of the Breast, though not unknown in men, are very much more commonly seen in women. The most usual cause is, undoubtedly, suckling infants with either hereditary or acquired syphilis; other methods of infection are kissing or biting by an infected individual, or by the so-called custom of 'drawing the breasts' to empty them of milk either by the mouth or by an infected instrument. Chancres of the breast may be single, but are often multiple. Fournier gives a case with twenty-three distinct chancres, sixteen of which were on the right breast and seven on the left. In 1899 Danlos recorded a case of a woman, aged thirty-four, who noticed pimples on her breasts one week after the death of a syphilitic child she had been nursing for a month. She had a superficial ulceration on the left breast which was somewhat saucer-shaped and indurated, while on the right breast there were twenty-one distinct ulcers, each about the size of a lentil, most of them being covered with crusts. The glands on the thoracic walls of the axillae were enlarged and indurated. One week later several of the ulcers had fused together, and the number was now reduced to eighteen.

This case illustrates several facts in connexion with breast chancres, first that (1) both breasts may be infected. (2) Here we find a single lesion on the left breast, and twenty-one on the right, thus showing the multiple character of the lesion. (3) The infant had been dead a week before the sores were noticed, and by that time they were incrusted. (4) Suckling prevents this incrustation, and the moisture maintains the erosive condition of the sores. (5) The single ulcer on the left breast was a superficial, saucer-shaped, indurated and typical chancre. And last and perhaps the most important point in the diagnosis of any extra-genital chancre, the position and condition of the lymph glands.

The sore or sores may be situated on the nipple, on the sulcus which divides this from the areola, or on the breast itself. The chancre may be of the erosive or incrusted type, or occasionally may be found as an indurated fissure. The induration is, as a rule, marked, and exactly underlies the little ulcers. If situated on the nipple it will either be in the form of a flattened papule or may be a distinct nodule; while if in the sulcus the lesion is generally multiple and the series of sores may assume a circular form. The glands involved are those of the thoracic wall of the axilla. If the sore takes the form of an indurated fissure, some difficulty may be met with in diagnosing the condition from that of an ordinary fissure: but it should be remembered that the chancre may be painless, although the true fissure is as exquisitely painful as a fissure of the anus. The patient cannot allow it to be touched or the child to suckle from that breast. These fissures readily become septic, and one may find inflammatory lymphatics extending towards the axilla; they bleed most easily. But, provided sepsis be avoided, the glands are not generally involved.

Finally, in arriving at a diagnosis with respect to any sore of the breast, the possibility of its being an extra-genital chancre must never be forgotten. Too often, indeed, this point is overlooked. Syphilis, as a cause of these anomalous ulcerations, if thought of at all, is usually the last point to be considered.

Digital Chancres. These lesions in women are found most commonly among nurses and midwives, being acquired in the course of their duties, and especially perhaps among those who suffer from an eczematous condition or dermatitis of the fingers, the result of the constant use of irritating lotions, &c.

Bulkley records the case of a lady who acquired a chancre about the nail of the ring-finger from dressing a sore on the eyelid of a relative. Robbins relates how a little girl fell down and hurt her finger; an uncle, who had mucous plaques in his mouth, sucked the wound and so infected his niece.

Of all extra-genital chancres, digital sores most frequently remain undiagnosed until the appearance of secondary lesions, and even then so ephemeral are they, that in some cases they may absolutely escape notice ; in some cases there is no pain, and the only sign at the seat of inoculation is a small dusky spot or brownish stain. In Jullien's case already quoted, it will be remembered that, though general infection followed a small punctured wound into the pulp of the finger, no sign of a chancre was at any time discoverable.

As a rule, however, a digital chancre is a well-marked lesion, differing from other primary sores in many ways. It varies so much in appearance that it is impossible to speak of a typical digital chancre. It is impossible to make out any induration of the floor or edges in the majority of cases, this being probably due to the extreme density of the tissues affected. There is often a general swelling of the part, but this is also found in simple inflammation. This absence of induration is so common in digital chancres as to constitute a fact to be particularly remembered. The lesion is very rebellious to ordinary treatment, and is very indolent and persistent ; cases have been recorded where the chancre has lasted many months. It may be single or multiple, it is very prone to septic influences, and may suppurate freely. The nail is often destroyed, and if the lunule be affected it may not grow again, or only in a malformed fashion, and considerable deformity of the finger-tip may result. The glands involved are those high up in the axilla, and, since the sore is not uncommonly septic, these may suppurate. The epitrochlear set of glands will be involved in cases of sores on the little finger and inner half of the ring-finger, occasionally also with sores on the other fingers, this being probably due to the free anastomosis of the lymphatics.

The sore will generally be found on the dorsal aspect of the phalanges, in preference to the palmar, and especially about the nail, 'hangnails' affording a favourable point of entry for the virus. Such sores are often extremely painful.

Taylor, of New York, describes four ordinary varieties : (1) the excoriated nodule ; (2) the fungating sore ; (3) panaritium-like chancre ; (4) the scaling papule or tubercle.

The excoriated nodule starts as a small pustule in a fissure or 'hangnail', and, though indolent at first, it becomes in a few weeks a large, fleshy, smooth or granular, dull red or purple mass. The pain is often continuous; the nail may be hopelessly destroyed, and great deformity result.

The fungating chancre, an exuberant growth affecting the pulp of the last phalanx, may suppurate freely, is very tender, and prone to bleed.

The panaritium-like chancre, or 'chancre panaris' of Fournier, is often mistaken for a whitlow; the edges of the ulcer are undermined; the surface may discharge pus; the pain is excruciating and they are very indolent. In a case given by Jacobson the incubation period was three months from the date of infection to the first appearance of the sore, viz. April 16 to July 14.

They often assume a semilunar shape round the nail, which is eventually destroyed, and on healing marked malformation of the finger-tip remains.

The scaling papule or tubercle begins as a small red spot, which grows rapidly till it has a diameter of about half an inch, may be found on any part of the phalanx; but if a flexure of a joint be affected, it then becomes rather an indurated fissure. Taylor says this form is very rare, but this is possibly due to the fact that, of all digital chancres, it gives rise to the least discomfort or pain, and is very often overlooked. Its duration is from a few weeks to several months, and it leaves behind it only a small brownish pigmentation.

Chancres of the first and second phalanges are often flat, non-indurated, callous, and very chronic ulcerations, which may occupy the whole of the dorsal aspect.

The diagnosis of syphilis is usually a difficult one to establish: if there be much suppuration, the typical condition of the glands may be quite masked by the results of the septic absorption, and it is not rare in these cases for an axillary bubo to form.

Treatment. Arrest the inflammation with hot boracic lotion, mercurial ointments, and, if syphilis be the cause, get the patient under the influence of mercury as speedily as possible.

CHAPTER XX

THE EARLY MANIFESTATIONS OF SECONDARY SYPHILIS AS SEEN IN WOMEN

With the establishment of the chancre and the involvement of its anatomically related glands we pass to the second stage of the disease, the period of the dissemination of the poison throughout the system.

As with the primary lesion, this eruptive stage, as it has been called, is preceded by an incubation period, the average length of which is forty-five days, that is to say, from the appearance of the chancre to the outburst of cutaneous secondary lesions. But during this stage the virus is no more idle and inert than it was in the period antecedent to the appearance of the chancre. The poison, while still availing itself of the lymphatic system as a means for reaching distant parts, as evidenced by the enlargement of the lymph glands in situations often far removed from any eruption, or ulceration, now seizes on the vascular system as an additional and more rapid method for its general distribution.

Thus it spreads further and further towards the surface, upon which it breaks out in the form of macules or papules, or both. The somewhat rounded form of the different parts making up such an eruption, has been compared to the base of an inverted cone, the apex of which is situated at the point whence the bunch of small vessels arises from the terminal main trunk, which is now more or less obliterated by a collection of the specific organisms, and by the endarteritis which, through the toxins produced, they give rise to. This incubation period may be prolonged beyond the normal by the institution of specific treatment. Many women pass through this period quite unconscious that anything is the matter with them, while in others the circulating virus produces a more or less severe general disturbance: e.g. malaise, lassitude, fever, neuralgia of various parts, especially of those supplied by the fifth cranial nerve, headaches, at times continuous and severe in the evening or night time, cachexia and general wasting, which may be great, osteocopic and rheumatoid pains (which, like the headaches, are often nocturnal), transient albuminuria. The urine should, therefore, always be tested before starting specific treatment, because mercury can only be given with great precautions to a patient with chronic albuminuria.

A universal enlargement of the Lymph glands, superficial, and probably the deep, is occasionally the first effect of the general invasion of the system. This condition will be found in thin, spare people, and especially in those with tubercular tendencies. I lately saw a case in whom, previous to the outbreak of any secondary eruption, almost every superficial gland in the body could not only be felt, but could be plainly seen. The different glands were smooth, hard, indolent, discrete, not of any great size, and the unaffected skin was freely movable over them. This general enlargement of the lymph glands was, at the time, the only confirmatory evidence present as to the nature of the chancre, the whole forming as perfect an illustration of the superficial lymph glands of the body as one could wish to see.

In women much more frequently than in men do we find, as evidence that the system is being invaded, *condylomata lata* in the neighbourhood of the genital initial lesion. It is, however, surprising to find, even in the most recent literature on venereal diseases, how many syphilographers still speak of this condition as part of the primary lesion. A condyloma latum is only a papule modified by its environment. I consider I am well within the mark in stating that in quite sixty per cent. of the women attending the Lock Hospital with early syphilis this early condylomatous condition will be found.

This outbreak of an early papular syphilide in the neighbourhood of the chancre is too common an occurrence to be considered a mere chance coincidence. A little consideration will show that it is in reality a question of cause and effect.

Whether syphilis be acquired from a primary or secondary lesion the result is the same, a chancre. Now this chancre is the great and at first the only centre for the distribution of the toxins and colonies of the specific agent throughout the system. Moreover one of the arguments advanced in favour of excision of the primary sore, in days gone by, was that by this operation the principal nidus of the poison was removed. But these theorists omitted to take into account the rapidity with which the poison permeates the tissues and gives rise to fresh colonies elsewhere. In the chancre, then, the intensity of the poison reaches its maximum, and, given favourable conditions, to be presently mentioned, breaks like a storm on the neighbourhood of the place of its birth. The greater the distance from the original focus, the less intense will be the effects produced. Often, indeed, in a case of a genital chancre, the whole vulval aspect is a mass of condylomata lata, extending, it may be, posteriorly around and within the anus, affecting at times the vaginal walls and even the cervix uteri, reaching anteriorly on to the mons veneris, and laterally on to the sides of the thighs. But, outside the area affected by this condylomatous 'storm', one finds only a few scattered ordinary dry papules.

The same law holds good for what may be called the results of syphilis. After a syphilitic man marries, both he and his wife may be anxious to have a family. The wife is infected by her husband; the result may be a long series of disasters before a healthy, non-affected child is born. Miscarriage follows miscarriage; then perhaps abortion; the birth of a still-born child, or child born alive but immature, and only surviving a few days; the next child born alive and apparently healthy, but in a short time developing symptoms of congenital syphilis; finally, a healthy child is born who may never in the course of his life show any signs that he is afflicted with the family taint.

We are only working in a circle; the same law is common to both cases. The intensity of the poison will be found to vary directly as the distance from the original focus of the disease.

Hallopeau says that every local proliferation constantly plays a preponderating part in the genesis and development of syphilodermata. In each of them a pathogenic agent, introduced into a part of the organism, multiplies and gives rise to toxins, which are the immediate cause of the local reaction. Presently it propagates itself from place to place, either by the lymphatics or by the interstices of the tissues, to a greater or less distance from the initial lesion, to give rise there to secondary symptoms, which in their turn become fresh centres. The lesions provoked by these intra-inoculations vary according to the period in which they are produced. And so he has formulated the following law: 'Every local manifestation of syphilis in a previously unaffected part shows a pathogenetic activity greater than the secondary deposits, which reach the part by intra-inoculation. And if there be many of these successive generations, each one of them will be found to be of less intensity than its predecessor.'

This outbreak of condylomata lata in the neighbourhood of the initial lesion will be found to precede by some days the appearance of secondary lesions elsewhere.

Whether in a woman the early manifestations of syphilis take the form of a slight roseola or of a more or less marked papular eruption, will depend principally on her powers of resistance to the poison, and in the majority of cases with condylomata lata a more or less severe papular eruption will follow later.

The conditions most favourable to the growth of these lesions are—any cause which tends to lower the resistive power of the patient, e.g. want of cleanliness, sepsis, pregnancy, &c. These growths may be few or many, when they often become confluent, covering a large extent of surface. Once recognized, a mistake can hardly be made as to their nature. They are flat, red or dirty grey, moist, granular disks, apparently glued on to the surface. They are in reality oedematous papules in which a considerable hypertrophy of the prickle cell layer has taken place (see Plates LIII and LIV).

Condylomata acuminata, often found in syphilitic patients, are due to other causes—gonorrhoea, pregnancy, &c.

The *roseolar or macular syphilide* is due probably to the toxins circulating in the blood, and is made up of more or less numerous, irregularly rounded, pinkish-red spots or patches of about half an inch in diameter, scattered over the surface of the body (see Plate XLI). These spots remain discrete, showing no tendency to coalesce or to form rings, except in the somewhat rare case of a circinate erythematous syphilide, when they do both.

The eruption is generally first seen about the sixth or seventh week after the appearance of the chancre. It comes out in crops, taking about seven days to reach its maximum. The first appearance will often be found about the umbilicus and abdominal wall, whence it spreads over the body. Not infrequently, and in women especially, the inner aspects of the thighs will, if examined with the light shining obliquely on them, reveal the beginning of the eruption under the skin before it is visible on the surface. This part may be readily inspected during the examination of the genital organs.

The back is another very favourite seat for this or any other syphiloderm. This is a point on which too little stress is laid by syphilographers, but so often do I find an eruption better marked on the back than on the chest and abdomen that I frequently examine this part first, before inspecting the front aspect. This examination of the back may give rise to some difficulty with women, but the trouble may generally be overcome by pointing out to them that often an eruption shows a special proclivity for certain parts and the necessity for arriving at a correct diagnosis as early as possible. Many a case will have a marked eruption on the back and show no evidence whatever of any on the chest or abdomen. It was formerly thought that syphilitic eruptions affected the softer, less exposed flexor, in preference to the extensor surfaces, thus the back, owing also to the inconvenience of undressing, was often not examined.

Several variations from the type have been observed with this eruption. Its onset may be, and often is, preceded by a more or less marked feverish disturbance; but in many cases the patient is quite unconscious of its presence until the doctor calls her attention to it, owing possibly to the fact that there is no itching, discomfort, or other subjective symptom. In some rare cases itching may be more or less pronounced. Any cause which increases the cutaneous congestion may suddenly call the eruption forth; e.g. alcohol, exercise, hot baths, &c. Bumstead gives a case of one of his patients who took a hot bath just previous to going to a ball;

this brought out a profuse roseola on the face and neck, which was recognized by several of the patient's associates. I have seen alcohol produce the same effect very suddenly, and with disastrous effects so far as the patient's after-prospects in life were concerned.

Again, the eruption may be so slight and evanescent as to entirely escape detection. It has been observed that if the eruption start early, its duration may be from a day or two to six weeks. If it be late in appearing it may last several months, and this in spite of treatment ; or it may relapse several times. In the early stages the colour may be completely driven out of the macules by the pressure of a lens, but later a yellow-brown stain is seen. This, however, is not peculiar to syphilitic eruptions, but will be found with many other chronic skin conditions.

Sometimes the hyperaemic condition is more pronounced. The individual macules are then of a deeper tint, better defined, and resemble rather immature papules. This condition is found on the palms of the hands and soles of the feet, and marked desquamation may occur in these situations, although, as a rule, a typical roseola does not scale, or, if it does, the desquamation is very slight.

Another form the eruption may take is that of the circinate erythematous syphilide ; here the various elements fuse together to form large and often complete rings of an inch or more in diameter. These rings, having somewhat speedily reached their full development, show no further tendency to increase peripherally. The condition more especially affects the face, neck, shoulders, and axillae; it is often found in association with seborrhoea, and is very prone to relapse. Such relapses may be very troublesome to the patient for several years, since they occur on such prominent places as the face and neck, they are not infrequently chronic and rebellious to treatment.

As I have not seen a case of this condition in women for some time, I give an example from the notes of my male out-patients as illustrating the chief points above alluded to.

CASE 14. ——, a bootmaker, single, aged 39; a small, spare, thin man ; weight 9 st. 2 lb.

July 22, 1907. Attended the hospital with phimosis, a concealed chancre, inguinal adenitis, and a roseola of five days' duration, which affected especially the back of the neck and upper part of the trunk. I marked this especially in my notes to see whether he would later develop a pigmentary syphilide of the neck. Infection had taken place exactly six weeks previously. On October 21 his weight was 8 st. 11 lb., and he told me that a few days previously a ringed eruption on the lower part of the face and neck had appeared rather suddenly. Within forty-eight hours of the onset, the rings had reached their full development, and showed no further tendency to increase peripherally. The eruption had started in the moustache near the right angle of the mouth. On inspection, the rings, which were one inch in diameter, and complete, were found in the following situations: one below the centre of the left cheek, another at the right-hand corner of the moustache, others over the pectoralis major, where this forms the anterior wall of the axilla on each side, and others on the dorsal and lateral aspects of the neck. The rings were considerably raised above the surface of the skin, and were of a bright pink-red in colour; they were not irritable, but soon after their appearance they were covered with a white pellicle.

November 8. The weight was 8 st. 5 lb., and a fresh ring had just started on the left buttock.

November 18. Weight 8 st. 6 lb.; all the rings were disappearing.

November 25. He was not so well, and the eruption was again becoming evident. With the exception of the loss of weight, the eruption was not ushered in by any preliminary symptoms of malaise, &c.

November 28. The ring on the buttock had disappeared, and the others were all breaking up.

For many years the patient had been troubled with 'dandruff'. This form of roseola is said to be most frequently found in patients with some form of seborrhoea.

The Diagnosis of the Macular Syphilide. In almost every case of this eruption we shall find confirmatory evidence of the disease in other parts, e.g. the chancre may be still present (less frequently so in women than in men), adenitis is constantly present, and in many cases a papular eruption will be found mixed with the roseola.

But with a slightly marked or evanescent case it has been suggested that compression of the seat of a doubtful roseola by an elastic band will, in the course of a few minutes, cause the spots of such doubtful eruption to become red, copper-coloured, and livid, the venous compression bringing about an overfilling, dilatation, and congestion of the affected parts.

Very considerable assistance is derived from the use of a cobalt-blue glass. This method was first suggested in 1893, by André Broca. It is a question of complementary colours, and so it will be necessary to isolate the examining eye from the influence of all white light. For this purpose, since reading Jullien's article in 'Les Annales de Dermatologie et de Syphiligraphie, 1899', I have used cobalt-blue spectacles with side pieces. A dullish day in preference to one with bright sunshine should be chosen, and it will be seen, as Jullien has shown, that, 'By thus isolating the eye, the epidermis appears of a uniform blue colour, but if in the thickness of the integument there be red congestive areas impossible to distinguish in the surrounding white light, the red congestive cutaneous colour will appear, because it is complementary to cobalt-blue, and clinically we get either (1) the picture of an eruption before the unaided eye perceives it, or else (2) evidence of an obliterated eruption.'

These 'roséoles à verre bleu', as they are named at the St. Lazare Hospital, may be of very great assistance in arriving at a correct diagnosis. A macular roseolar eruption may be confounded with the marbling of the skin so often seen in patients as the effect of cold and exposure, and which disappears as the part gets warm again;—with non-syphilitic erythematous eruptions, drug rashes, antipyrin, copaiba, even mercury in some rare cases, &c.—all of these are more markedly inflammatory than the case under consideration—with tinea versicolor, which is a fungoid growth on, and not of, the skin; scrapings of this may be microscopically examined, and the *microsporon* demonstrated—lastly with pityriasis rosea, which frequently gives rise to doubt or error in diagnosis. But here the absence of concomitant symptoms of syphilis, the branny scaliness of the lesions, and the presence of the primary mark will aid one in forming a correct opinion.

The *pigmentary syphilide of the neck* (see Plate LV), according to Sir Alfred Cooper, Stelwagon, Bangs, and Hardaway, is a rare manifestation. But in my experience, certainly among hospital patients, it is one of the most common of all the early manifestations we meet with. In my hospital notebook for the year 1904, in the first fifty consecutive cases of syphilis in all stages, the condition was found in thirty-seven cases, or nearly seventy-five per cent., and of the thirteen not showing the lesion, nine were cases of quite early syphilis, only the chancres and indurated glands being present, so that I have probably understated the real percentage. The ages of the patients were as follows :—

From 17 to 20 there were 15 cases.
,, 21 ,, 30 ,, ,, 13 ,,
,, 31 ,, 40 ,, ,, 4 ,,
,, 41 ,, 50 ,, was 1 case.
At age 51 ,, ,, 1 ,,
,, ,, 53 ,, ,, 1 ,,
In two cases the ages are not recorded.

In thirty-four out of the thirty-seven cases the colour of the hair and eyes was noted :—

Dark brown hair in 13 cases	Eyes brown	in 8	cases
	,, grey	,, 5	,,
Brown ,, ,, 3 ,,	,, grey	,, 2	,,
	,, brown	,, 1	case
Light-brown ,, ,, 11 ,,	,, blue	,, 3	cases
	,, grey	,, 6	,,
	,, brown	,, 2	,,
Flaxen ,, ,, 2 ,,	,, blue	,, 1	case
	,, brown	,, 1	,,
Black ,, ,, 4 ,,	,, grey	,, 2	cases
	,, brown	,, 1	case
	,, blue	,, 1	,,
Gray hair in 1 case aged 53	,, blue	,, 1	,,

Stelwagon, Bangs, and Hardaway think this condition is more commonly seen in brunettes. Sir Alfred Cooper found that dark women rather than fair are more likely to be affected, and the above table rather confirms this. R. W. Taylor says the condition is commoner in blondes up to the age of thirty or thirty-five.

This pigmentation may clear up in two or three months, but often it is very chronic and of long duration; it may persist for years, as it is often very rebellious to treatment. It is most frequently syphilitic in origin; I can only recall two or three cases in the last few years in which I was unable to satisfy myself of the presence of syphilis past or present. A well-marked case may be a source of great distress in women. The condition is rare, though by no means unknown in men. It occurs perhaps more frequently in those whose early symptoms are slight or not severe; there are no subjective symptoms, and many unobservant women, especially hospital cases, are quite unconscious of its presence until it is shown them, or they may tell you that their friends have remarked on their dirty necks. It is very seldom (most authorities think never) seen with congenital syphilis. The following case is interesting as showing the pigmentary syphilide in a probably congenital case who later acquired syphilis:

Case 15. ——, aged 20, single, height 4 ft. 5 in., weight 7 st. 6 lb., was admitted into the hospital November 2, 1904. In general development she was fairly well nourished but had the appearance of a congenital syphilitic. She stated that she enjoyed good health, except that as a child she had suffered with her eyes. On admission the signs of old interstitial keratitis were well marked in the right eye. The bridge of the nose was broad and depressed, the teeth were normal, but the soft palate was destroyed and cicatrized. She had one child, eighteen months old and healthy. There were multiple sores on the labia majora, indurated inguinal and cervical glands; a fading macular eruption on the inner aspect of the thighs, back, and abdomen; over the fifth cervical spine was a typical papule, in addition to the roseola. There was a condyloma latum at the umbilicus. The gums were sore and spongy. She had been treated for two months before admission. By November 11 she had developed a pigmentary syphilide of the neck.

The pigmentary syphilide generally starts and will be found most pronounced at the back of the neck, whence it spreads along the lateral aspects towards the mid-line in front and may extend towards the axillae. It is generally confined to the neck, but may cover nearly the whole trunk. Of the series of thirty-seven cases I have quoted from, in only two was the pigmentation noticed on the abdomen and back, in addition to being present on the neck.

It is seen in two well-marked forms :—

(*a*) A well-marked broad band of pigmentation extending round the neck—the collar of Venus—this was found seven times in the thirty-seven cases.

(*b*) Leucodermic patches surrounded by a network of pigment—these were found thirty times in thirty-seven cases.

The first variety may be, although not invariably, the preliminary stage of the second.

Taylor describes three forms :—

(1) Spots or patches of various sizes.
(2) Retiform pigmentary syphilides.
(3) The dappled or marmoraceous.

Hardy called attention to the condition in 1853, and Fournier in 1873, and much has since been written to explain the various theories advanced to meet the question. Not so much *why* a woman with syphilis should get the deposit of pigment so frequently seen in the cervical region, but rather *how* it is produced.

The substance deposited is melanin, and not blood pigment. In cases of sunburn the deposit of pigment is regarded as a defensive act on the part of the organism against the effects of the actinic rays of the violet end of the spectrum. We also see a somewhat similar effect produced by certain toxins acting from within, e.g. arsenic, and by certain diseases besides syphilis, viz. Addison's disease, diabetes, &c. Ehrmann says the melanin is manufactured by special cells called melanoblasts, which are derived from the same embryonic layer as the connective tissue cells, from which they are early differentiated. Further, he determined in twelve cases of this condition that, in the leucodermic spots examined soon after their appearance, the melanoblasts were larger and more numerous than in the neighbouring parts. In the leucodermic spots of longer duration there was a central zone in which the melanoblasts were entirely wanting, or only few in numbers, and small. The zone nearer the edge but still partially clear to the naked eye shows many large melanoblasts.

The questions on which syphilographers have been divided in opinion with respect to the pigmentary syphilide of the neck may be shortly put as follows :—

(1) Does the pigmentary network surround islets of normal skin ?
(2) Do the white islets present a true degeneration ?
(3) Does the pigmentation appear from the first as such, and are the white lacunae found later in this tissue ?
(4) Is the deposition in a network primary ?
(5) Does the pigmentation appear ‘ de novo ’ as such ?
(6) Is it preceded by an exanthem ?

In 1903, Hullen (Paris) made a series of examinations, the results of which may be summed up as follows :—

(1) Roseola of the neck is much more frequent than authors generally allow. It is sometimes very fugitive.
(2) Very often the pigmentary syphilide is produced in parts which have been previously attacked by secondary syphilides, roseola, &c.
(3) The chief part of the lesion, viz. that which causes its variation in form is the white spot.
(4) The achromic spots are the remains of a roseola or other secondary syphilide preserving the site, the form and dimensions of the lesions which have given birth to them. This he demonstrated by charts of the roseola or secondary syphilide, carefully prepared, previous to the deposition of thc pigment.

Finally, said Hullen, if one regarded the production of pigment as a defensive act against certain agents, notably organic poisons, then one must admit that the white zones are cicatricial relics, while the brown network would spring from the migration of the pigment occasioned by the syphilitic virus, whose distribution would be controlled by the modifications which belong to roseola and secondary syphilides in a cutaneous region.

In 1904, working on these lines, I convinced myself, often with aid of the cobalt-blue glass, that roseola of the neck is a not uncommon symptom. I satisfied myself, with charts, as to the correctness of observation No. 4. I have often watched the different elements of a syphilitic eruption of the neck clearing from the periphery to the centre, and this latter point may often be seen occupying the centre of the sclerotic spot after the formation of the pigmentary network. Of the thirty-seven cases I have already alluded to—

In 15 an eruption preceded the pigmentation.
3 were admitted with roseola and pigmentation.
4 were cases of marked darkly pigmented collar—no eruption evident.
3 were cases of pigmentary syphilide in old tertiary cases.
5 were cases of pigmentary syphilide with fading eruption on back.
2 were cases of pigmentary syphilide followed by an eruption on the neck.
5 were cases of pigmentary syphilide. No eruption evident.

Remembering how evanescent roseolar eruptions may be, and how often they relapse, I certainly consider that in the majority of cases, if not in all, the pigmentation is secondary to a previous eruption. The chief difficulty is with the cases of dark pigmented collars. I have watched these break up into a network without being able to find any signs of an eruption past or present.

CHAPTER XXI

TREATMENT

The Treatment of Syphilis. This question resolves itself into two chief parts: the treatment of the patient, and the treatment of the disease. No two individuals are alike in their reaction to the poison or to the remedies employed. Increase the powers of resistance to the poison and our chances of successfully fighting the disease are vastly increased. The only definite rule that can be laid down is to treat the complaint, when once it is diagnosed, as energetically as is compatible with the health of the patient. One of the greatest difficulties met with in treating women who are private patients is that very often circumstances are such that we are debarred from informing them of the true nature of their ailment. The treatment lasts a minimum time of two or three years. It is not merely treatment of symptoms as they occur, but the necessity for carrying on the treatment for long intervals without any outward sign of the disease, which forms the chief difficulty met with in both sexes, but, perhaps, especially in women. We know well—and wherever the opportunity occurs, it is our duty to impress our knowledge on patients; that the more thoroughly treatment is carried out during the first two or three years, the less will be their chances of being troubled in later life. Fournier and others have published statistics showing definitely that, in infinitely the greater proportion of tertiary lesions, the patients had been inefficiently treated in the early stages.

Syphilis, as a disease, is equally serious whether the earlier symptoms be slight or severe. Indeed, a so-called slight attack, owing to the likelihood of treatment being neglected, is, from the view of prognosis, often more serious than one in which more markedly severe symptoms convince the patient that she really has a serious ailment. Under no circumstances should a course of antisyphilitic treatment be started before a definite diagnosis of syphilis shall have been made. No particular harm accrues to the woman by waiting, and the interval may often be most profitably occupied by improving the conditions under which she may have to fight the disease.

Advantage may be taken of the interval to get the teeth attended to, and the general hygiene of the mouth improved. If there be troubles of digestion, these may be attended to. If stimulants be freely taken, these must be much curtailed, or better still, if possible, cut off altogether. It is often easier to stop stimulants, taken unnecessarily and perhaps in considerable quantity, suddenly, than by gradually doing so. If the woman be a cigarette smoker, this habit should be stopped. Tobacco, perhaps by its action on the circulatory system, is a well-recognized provoker of secondary symptoms. Any leucorrheal or other discharge should be treated and the patient advised to keep herself as clean and dry as possible.

When once syphilis is diagnosed, the earlier a course of treatment is instituted the better for the patient; the objects of such a course being to destroy the specific agent, to annihilate the toxins, to render the patient immune to their action, to treat the lesions they give rise to, and to prevent the transmission of the disease in either the acquired or hereditary form; never forgetting that the greatest assistance to the bringing about of these results will be derived by improving the powers of resistance of the patient against the poison.

The chief ways of administering mercury are: (1) by the mouth, (2) by inunction, (3) by fumigation, or (4) by the method of injection: and it may be advisable to use any one or all of these methods during the course of treatment of a case according both to the state of the disease and the susceptibility of the patient.

It is very difficult to lay down any general laws for the treatment of syphilis. We are endeavouring to meet the attacks of one poison by introducing into the system a second. It is now generally recognized that the successful termination of a course of treatment does not imply that a certain number of pills or quantities of medicine have been swallowed or a fixed number of injections, inunctions or fumigations have been made. And though it is of importance to impress upon the patient the necessity of strictly following the line of treatment prescribed, it is equally necessary to convince her that the last thing required is, that she should look upon herself, as is too often done, as an outcast, a leper or a chronic invalid. It is a question of education and winning the patient's confidence. If the patient will not help her medical adviser the disease almost invariably makes serious headway. A very great deal may be effected by fresh air, plain, wholesome food, the avoidance of late hours and excitement, and the freedom from, so far as possible, troubles and anxieties.

In very many cases this condition is only brought about by the assistance of suitable tonics, the use of a certain amount of alcohol, &c.—in fact what may be called auxiliary treatment.

If the mercury be pushed too far, that is to say to a greater extent than is necessary to meet the attack of syphilis, the patient will have two poisons to contend against, her powers of resistance will be lowered, and the severity of the attack will be found to vary directly as this resistance.

Among the symptoms of mercurialism, or danger signals, as they may be regarded, that the patient is taking more of the drug than is necessary to fight the disease in her particular case, are :—certain mouth conditions : salivation, gingivitis, &c.; disturbances of the alimentary system : purging, vomiting, anorexia, diarrhoea, &c.; disturbances of the general nutrition : loss of weight, lassitude, mental disturbances, &c., as well as certain symptoms due directly to the mercury : eruptions of the skin, muscular tremors, &c. Salivation and gingivitis may often be prevented by proper attention to the mouth before starting treatment; tartar, carious teeth, &c., may be removed or stopped. Whenever possible, it is better to postpone the use of mercury for a week or ten days while the mouth is being put in order—and the patient should be told to inform the dentist of the nature of her ailment. The teeth, &c., having been attended to, the patient must be impressed with the necessity for strict attention to oral hygiene during the whole course of the treatment. The teeth should be cleansed three times a day with an antiseptic dentifrice, the teeth being brushed up and down and not transversely, as the intervals between them are thus better cleansed of food particles, &c. Should the gums become affected by the treatment, the drug should be abstained from absolutely for two or three days, and the mouth rinsed out every few hours with an alum solution. Mercury may generally then be resumed either in a smaller quantity or a different preparation used.

Disturbances of the alimentary system as evidenced by pain, diarrhoea, &c., may at times be met by more careful attention to diet, e.g. the avoidance of coffee and alcoholic drinks, &c.; by changing the preparation used, by combining it with opium, or by adopting a different method of giving it, as, for example, by inunction, or intramuscular injections.

Disturbances of general nutrition are not uncommonly met with, as shown by debility, loss of weight, &c. Here change of surroundings, tonics, and plain, wholesome food may do much in aiding the patient to take the mercury. The weight should be taken at regular and fairly frequent intervals. Very many patients improve greatly in weight and general well-being while under treatment. But loss of weight may certainly be accepted as an indication that the drug, in the form prescribed, is not agreeing with the patient, and that the disease is not being effectively encountered.

The Effects of Mercury on the Individual as apart from its Effects against the Syphilitic Virus. Among these effects may be mentioned the peculiar blue violaceous hue assumed by the mucous membrane of the mouth, especially of the tongue, soft palate, and pharynx, in some patients who are taking a slight overdose of mercury. In others I have seen generalized erythemata with small vesicular eruptions on the palmar aspects of the hands. Occasionally, in patients very susceptible to mercury, we find marked and general tremors.

Other patients will tell one that both the smell and taste of the mercury is a constant source of worry. But none of these above-mentioned symptoms are to be accepted as indications that the treatment of the disease is not to be attempted. It very rarely indeed happens that such difficulties are insurmountable, or that a patient cannot take the specific remedy in one form or another.

Patients taking mercury are peculiarly liable to chills, and the untoward accidents mentioned above are more frequently met with during the summer than the winter months.

Of the many methods of administering mercury, by the mouth, by inunction, by fumigation, or subcutaneously, each one has its special advantages, and any one of them may be required to arrest the different phases of the disease.

In an ordinary case, with no indications to the contrary, I generally start with the oral method. It is cleanly, practical, painless, and should untoward symptoms arise, may be readily omitted. The great disadvantage is, that we have only the patient's word, not always to be relied on, that the treatment is being regularly carried out.

In certain somewhat severe cases of early syphilis, such as badly ulcerated throat, or marked eruptions especially, if on conspicuous parts such as the face and hands, and in which the other methods of treatment are either contra-indicated or objected to, considerable benefit may be derived by prescribing the mercury in the form of a mixture with iodides, and here I may say I always use the sodium and ammonium in preference to the potassium salt, as I find these less frequently give rise to symptoms of so-called iodism ; such a mixture I order to be taken shortly after food, and, in addition, tell the patient she must sip a large tumbler of hot water, too warm to be drunk off, one hour before each meal. In certain throat or mouth cases, in which it may be necessary to make topical applications of mercury, patients should be warned, if they have gold crowns or stoppings to their teeth, of the unsightly appearance which may result from the amalgam formed by the combination of the gold and mercury; in such cases it may be better to paint or use a spray, rather than a gargle, to the affected part.

In those cases which it is thought necessary to bring under the full influence of mercury as speedily as possible, the inunction method is perhaps the best. It has, however, this great drawback—that the treatment can only be carried out by skilled hands, and therefore the patient should be in a home or hospital.

In cases of chancres of the cervix uteri, or in cases of pregnancy, the following method suggested by Riehl of Vienna may be practised. An ointment, consisting of equal parts of lanoline and lard, with 12 to 15 per cent. of mercury is made. Of this about three grammes are applied daily to the cervix. In those cases in which the daily application is either impossible or inconvenient, five grammes are applied every second or third day. The preparation is kept in position by means of a carefully applied tampon, and in order to prevent this absorbing the ointment it is necessary to render the tampon impermeable, by impregnating it with a mixture of two parts of glycerine to one part of tannin. Riehl's results were most satisfactory, thirty-six out of forty pregnant syphilitic women reaching full term.

The subcutaneous method, either the intravenous or intramuscular, is another excellent method of bringing a patient rapidly under the influence of the drug. Abadie, of Paris, thinks intravenous injections are particularly suitable for eye lesions. Fournier, as we have already said, calls the tongue the organ of calomel.

Personally, I only use subcutaneous injection in selected cases. I prefer to use the insoluble rather than the soluble preparations, and generally calomel or grey oil (the latter prepared either according to Lambkin's or Lafay's formula).*

Either of these, especially the calomel, may be very painful;

* Lafay's formula is as follows:—

Purified Mercury	40 grams.
Anhydrous Sterilized Lanoline . .	12 ,,
White Sterilized Vaseline . . .	13 ,,
Sterilized Vaseline	35 ,,

(Mercury 40%).

Two 5 to 7 centigrams of mercury must be injected.

Lambkin's Cream is made as follows:—

Mercury	10 grammes.
'Creocamphor'	10 cc.
Palmitin basis	100 cc.

1 gram of mercury in 10 cc. Dose 10—15 minims.

The cream should be warmed and well stirred before use for injections.

the pain may not come on for twenty-four hours after the injection, and for this reason many women patients object to the method.

Fumigation with calomel is a line of treatment not, in my opinion, sufficiently used in the present day. It is most suitable for the treatment of chancres, condylomata lata, and certain mouth and throat conditions, by means of an ordinary glass calomel fumigator, or for cases of multiple ecthymatous sores on different parts of the body by means of a calomel bath, as practised by the late Mr. Henry Lee.

This method cannot be used in many cases, if iodides are being prescribed at the same time, owing to the great pain and discomfort this mixed treatment often gives rise to.

In some rare cases it seems impossible to find a preparation of mercury suitable to the patient. Iodipin and the various iodides may then be tried, and if successful in getting rid of the early symptoms, then possibly the patient will be able to take mercury in some form or other. For it must be remembered that iodine and its preparations will not cure the disease, and that a large proportion of the cases of tertiary syphilis will be found to have been treated with iodides only.

Arthur Shillitoe

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Plate XLVIII.

Large ulcerated surface on each labium appearing after the eruption—no primary lesion discoverable. (Case 1.)

(*From a direct colour-photograph.*)

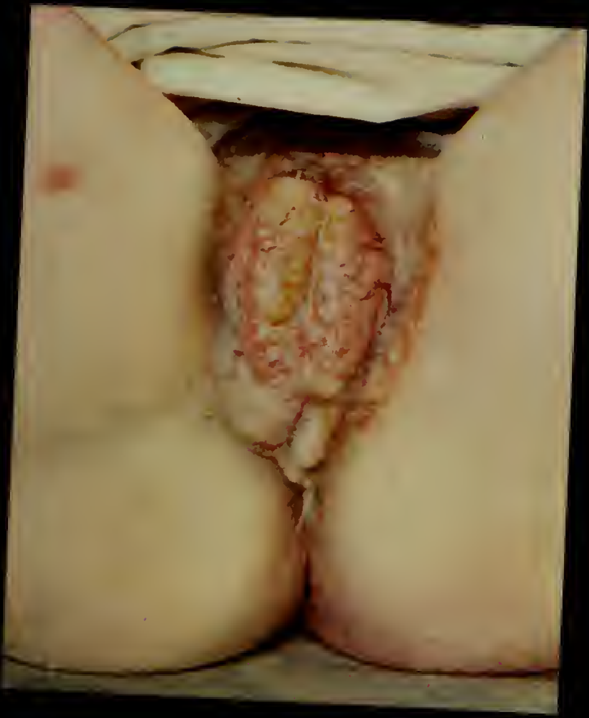


PLATE XLIX.

Phagedaenic sore. This began on the left labium majus, and in a few days extended to the right labium and inner side of the left thigh; there was no marked induration at any time; when first seen there was a marked papular eruption and enlarged inguinal glands.

(*From a direct colour-photograph.*)

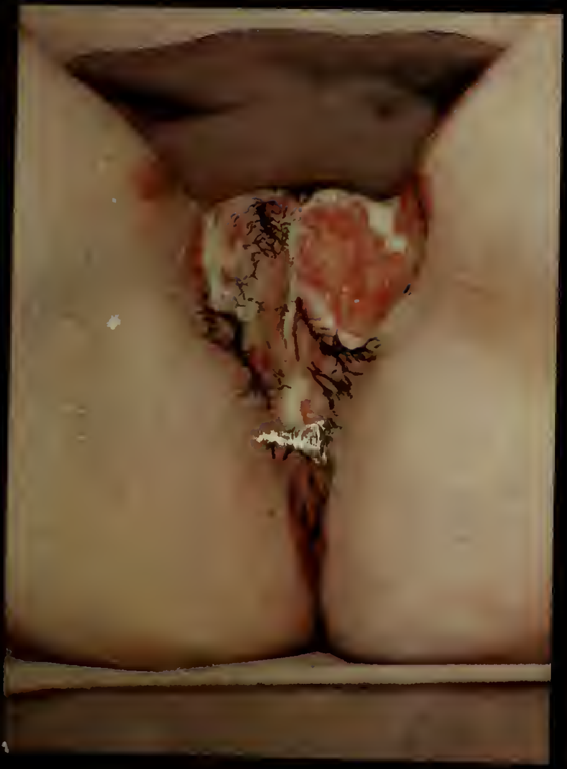


PLATE L.

Typical large flat primary sore of the posterior end of the right labium majus, with indurated oedema of the whole labium. There is a juxtaposed sore of the left labium majus.

(From a direct colour-photograph.)

Plate LI.

Multiple indurated sores. Two sores are seen at the posterior end of the right labium majus, another was found at the base of the clitoris, and a fourth on the left labium minus; indurated oedema is well marked in the left labium minus.

(*From a direct colour-photograph.*)

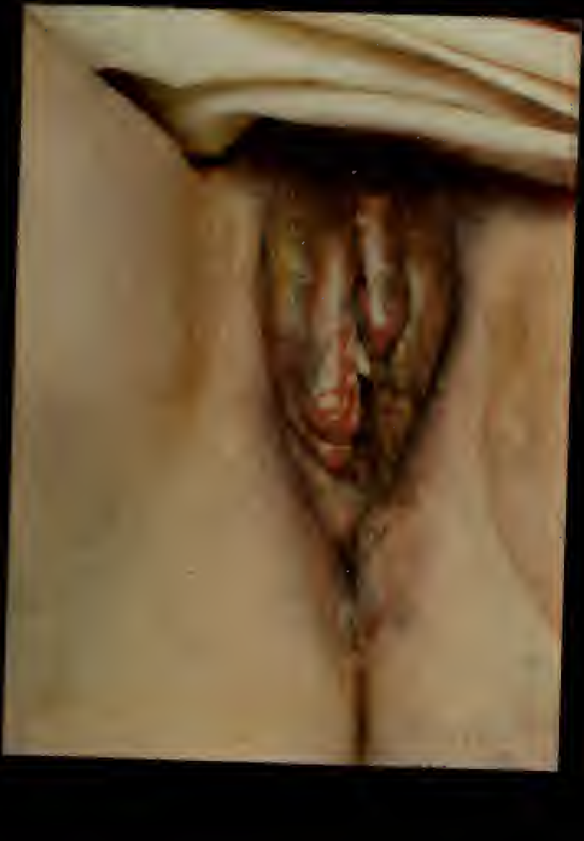


PLATE LII.

Chancre of the left half of the upper lip in a girl of thirteen. Infection from syphilitic infant, followed by general roseola fifteen days after diagnosis of chancre. (Case 12.)

(*From a direct colour-photograph.*)

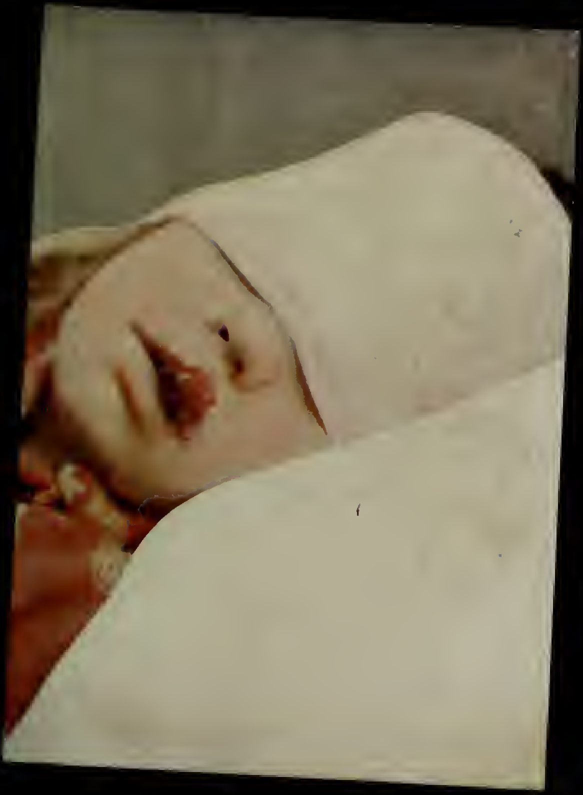


PLATE LIII.

Condylomata lata surrounding the vulva, secondary to primary indurated oedema of both labia majora. No other form of primary lesion was to be found.

From a direct colour-photograph.)

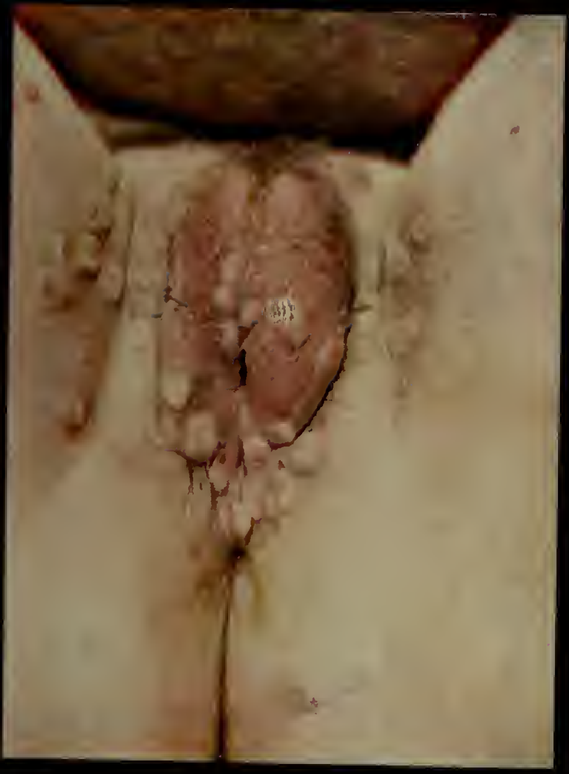


PLATE LIV.

Indurated primary sores in the middle of the left labium majus, and anterior part of the right—the outer surfaces of both labia being covered with condylomata.

(*From a direct colour-photograph.*)

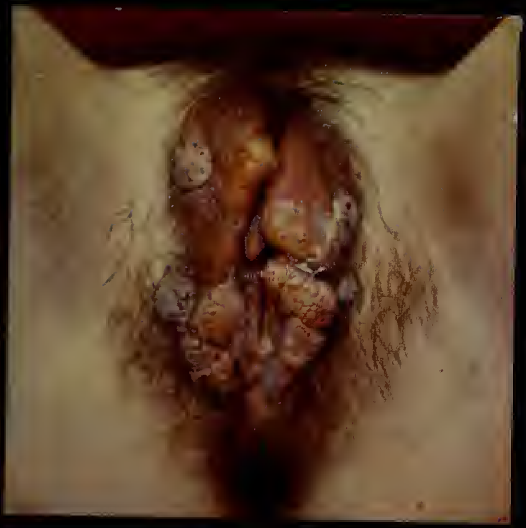
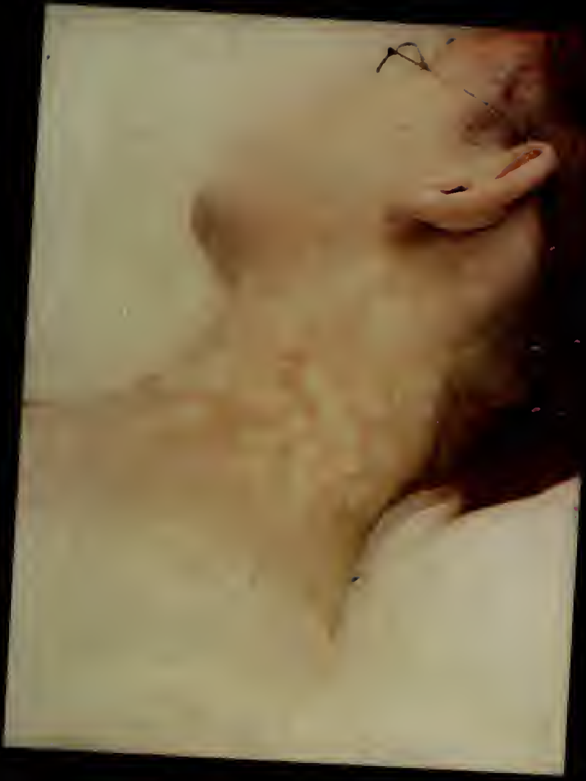


Plate LV.

Early pigmentary syphilide of the neck.

(*From a direct colour-photograph.*)



CONGENITAL SYPHILIS

BY

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CHAPTER XXII

HISTORY AND AETIOLOGY

Since Paracelsus in 1529 first asserted the existence of an inherited form of syphilis, many writers have added to our knowledge of the subject. The first actual record of its occurrence would seem to be in 1560, when Guillaume Rondelet (1507–66), the friend of Rabelais, wrote 'Hoc etiam in pueris natis ex matre vel patre infecto ostenditur. . . . Ego vidi puerum nasci totum coopertum pustulis morbi Italici'. (This is shown too in the children of an infected father or mother. I have seen a boy born with the whole body covered with pustules of the Italian disease). Ambrose Paré (1510–90) refers to the frequency of syphilis in infants 'who are born with this malady and on whose bodies numerous pustules appear soon after birth', but as Diday points out, this may not show that he recognized the inheritance of syphilis, but rather that he recognized that syphilis may be conveyed during birth, for he states elsewhere that 'syphilis is never observed to be transmitted from father to son'.

In the seventeenth and eighteenth centuries the belief in the inheritance of syphilis gradually gained acceptance, but was still not universal. Dr. Walter Harris (1651–1725), a London physician, who in 1689 published the first edition of his work 'De Morbis Acutis Infantum', which gained the strong approval of Sydenham, mentions the occurrence of syphilis in infants as an infection from their nurses, but only hints obscurely that syphilis in parents is responsible for 'certain transmitted diseases in the children' (hinc morbi aliquot puerorum tralatitii). During the later part of the eighteenth century, congenital syphilis was studied carefully by many French observers, and in the nineteenth century the works of Diday, Hutchinson, and others, have left little to add to our knowledge of the symptomatology of the disease.

Syphilis in infants may be acquired by contagion after birth; for instance, it has been transmitted by kissing from adults with syphilitic sores on the lips ; possibly, in rare instances it may be acquired by contagion from a syphilitic sore on the maternal genitals during birth, so that the term ‘ Infantile syphilis ’ would include more than inherited or congenital syphilis. In the present article only the inherited or congenital form of syphilis will be considered, and the terms ‘inherited’ and ‘congenital’ will be used here as synonymous. Some writers have attached a separate significance to them, using the former to indicate the transmission of syphilis at the time of conception, the latter to mean conveyance of the disease during some later period, that is, by infection of the mother during pregnancy. Such differences certainly exist, but it seems inexpedient to apply different terms to the disease according to the particular mode of transmission, for there is no clear evidence of any corresponding difference in its symptoms or course.

MODE OF INFECTION

The commonest mode of transmission is that to which the name ‘sperm infection’ has been applied; the father is syphilitic, the mother shows no evidence of the disease. It is indeed a remarkable fact that in the large majority of cases in which there is undoubted congenital syphilis in the infant, the mother has apparently had no symptom whatever of the disease, although her husband shows clear evidence of it. According to the statistics of Dr. R. J. Lee, in about 95 per cent. of cases of congenital syphilis the mother is free from all symptoms of syphilis. Three possible explanations of this curious fact suggest themselves : (1) that the mother has had symptoms so slight that they have been overlooked ; (2) that the mother receives from the foetus a modified form of the disease, which bears somewhat the same relation to the ordinary acquired disease that vaccinia does to variola, so that it causes no noticeable symptoms ; (3) that the mother receives from the infected foetus some material comparable to an antitoxin, so that although she does not contract the disease, she becomes immune. The immunity of the mother who has given birth to a syphilitic infant is an established fact ; it was observed by Colles in 1837, and embodied by him in the statement which is known as ‘ Colles’s Law ’ (sometimes also as Baumés’s Law, as the same fact was independently noted by him in 1840); it runs thus: 'A child born of a mother who is without any obvious venereal symptoms, and which, without being exposed to any infection subsequent to its birth, shows the disease when a few weeks old, this child will infect the most healthy nurse, whether she suckle it, or merely handle and dress it, and yet this child is never known to infect its own mother, even though she suckle it while it has venereal ulcers of the lips and tongue.' This immunity, however, cannot in the light of recent pathology be taken as proof that the mother has had the disease. It is quite conceivable that, as Coutts has suggested, the mother may absorb from the syphilitic foetus some antitoxin and 'so gain immunity herself, partial or complete. In this way such a mother, without having incurred the actual complaint herself, may have gained the position of one who has passed through and recovered from an attack of syphilis.' Whether the *Spirochaete pallida* proves to be the specific cause of this disease or not, the theory of maternal immunity gained from the foetus seems at least a plausible one.

It is hardly credible that all these mothers should have had syphilis without noticeable symptoms, when one considers how numerous and how obvious are the evidences of that disease, especially in its secondary stage in most cases where infection is known to have occurred; moreover, such mothers in many instances remain free from symptoms, and this without treatment, whereas experience shows that syphilis untreated, or even insufficiently treated is likely to show recurring and severe symptoms. The balance of evidence certainly seems to favour the view that syphilis may be transmitted from the father to the offspring, without necessarily infecting the mother, but the explanation of the mother's immunity remains uncertain. The fact observed by Guiseppe Profeta in 1865, and sometimes quoted as 'Profeta's Law' is noteworthy in this connexion: he stated that 'a healthy child born of a syphilitic mother could be suckled by her or by a syphilitic wet-nurse with impunity'—a fact which raises a very similar problem to that just considered, and which might perhaps with even more probability be explained by the transmission of some antitoxin from the mother to the foetus.

Next in order of frequency as a mode of transmission is infection of the offspring from syphilis in both parents at the time of conception. According to Hutchinson, such double inheritance only renders transmission more certain, but in no material degree intensifies the disease transmitted. Less often the father is healthy, but the mother has syphilis at the time of conception. If it be true that the father can infect the child without infecting the mother in the cases of sperm transmission which have been mentioned, the infection must be carried presumably by the semen direct to the ovum ; whereas, in the mode of transmission now under consideration the infection passes, no doubt, from the mother to the foetus in the maternal blood through the placental circulation. These two forms, therefore, paternal and maternal-infection of the foetus, or sperm and germ inheritance, are so fundamentally different that it might be expected that differences would be observed in the resulting disease in the child. Most observers, however, have found nothing in the inherited disease to characterize specially this or that mode of transmission. Lastly, the mother may acquire the disease at some date subsequent to conception, and transmit the disease to the foetus after several weeks or months of healthy intra-uterine life. For such transmission to occur, it is necessary that the mother should have been infected sufficiently long before delivery for the disease to have become generalized in her. Diday quotes cases illustrative of this mode of transmission, in which infection of the mother had taken place at dates varying from the sixth week up to the seventh month of pregnancy ; he held that the possibility of transmission was limited to those cases in which infection occurred between the end of the first month and the end of the seventh month of gestation.

Apparently no observer has recorded any facts which disprove this view, but it is difficult to believe that infection of the mother, however soon after conception, should be incapable of affecting the product of conception, though it is likely enough that a syphilitic infant may but rarely result, for where there is early infection of the mother early miscarriage will probably prevent the recognition of the transmitted disease.

Are there any factors in the mode or time of transmission which modify the disease in the offspring ? My own observations lead me to think that no modification in kind is produced in the symptoms of congenital syphilis by the mode of transmission; I have notes of every variety of transmission, but the symptoms of the disease show no special correspondence therewith. On the other hand, I think there can be no doubt that the more recent the syphilis, in one parent or in both, the more severe is the disease in the offspring. The liability to transmit syphilis evidently decreases as the interval since infection increases; it is generally agreed that parents who have reached the tertiary stage of syphilis are little liable to transmit the disease to their offspring, and probably the commonly observed decrease in severity of the transmitted disease in successive pregnancies points in the same direction. Such a history as this is common: (i) miscarriage at four and a half months; (ii) miscarriage at five and a half months; (iii) eight months' child lived two hours; (iv) boy who survived with well-marked symptoms of congenital syphilis; (v) apparently healthy when seen by me at the age of five months.

On the other hand, there are remarkable exceptions to this rule; the disease is sometimes much more severe in a later than in an earlier child; occasionally one or more children escape infection altogether, whereas a later child shows the disease; and lastly, several cases have been recorded of infection of one of twins while the other has been healthy. The following instance illustrates some of these points: (i) twin, premature, both still-born; (ii) survived, shows interstitial keratitis; (iii), (iv), (v) all miscarriages; (vi) apparently free from syphilis; (vii), (viii) still-born; I have no record of the subsequent children until (xiv), a girl, who came under my observation at six years and eight months with haemoglobinuria, a condition which in children is usually associated with syphilis.

One of twins under my observation died at the age of seven months with severe and fatal syphilis; the fellow-twin was apparently perfectly healthy. Sir Herman Weber published an instance in which a syphilitic mother bore twin children, one of whom suffered with characteristic symptoms of congenital syphilis, and died at the age of eleven weeks with diarrhoea, whilst the other remained perfectly healthy.

An important question which must be considered in connexion with the transmission of syphilis from parent to offspring is whether a person with inherited syphilis can transmit the disease to the next generation: in other words, is there any transmission of syphilis to the third generation? On *a priori* grounds there seems to be no reason why this should not occur, but there is an obvious reason why it should occur very rarely, if at all; and this reason arises out of the foregoing observations on the gradual diminution of the liability to transmit syphilis as the interval since the date of infection becomes longer. In the case of an adult with acquired syphilis, who has undergone thorough treatment, a period of four or five years at most is thought to be sufficient interval after the subsidence of symptoms to insure freedom from risk of infecting by marriage, and it is quite certain that in some cases even eighteen months of treatment is sufficient to prevent the transmission of the disease to the offspring; moreover, it seems certain that, whether treated or not, syphilis tends to come to an end in the course of years. It seems, then, only natural that in the many years which must elapse between the syphilization of an unborn child and the time when that child becomes a parent the liability to transmit the disease, even if present in earlier years, would already have become extinct; moreover, in the large majority of cases, some treatment will have been received in infancy, which must still further diminish the power to transmit the disease. It might, therefore, be expected that if syphilis were ever transmitted to the third generation it would be extremely rarely, and that this would occur chiefly when the parent with inherited syphilis had married early. In my own experience I have not come across a single instance of syphilis in the third generation, but a few cases have been recorded in which this was supposed to have occurred. One of the most convincing of these is that recorded by Mr. Hutchinson: a woman who married at the age of twenty years, having notched teeth, scars at the angle of the mouth, and 'unmistakable evidence of inherited taint', had an infant with obstructed nostrils and a copper-tinted scaly rash on the buttocks 'of the most unmistakable character'; the symptoms in the infant disappeared under mercurial treatment; the father appeared not to have had any form of venereal disease. Mr. Hutchinson himself, however, advised that this single fact should be received with great scepticism, and now, nearly twenty years after publishing this record, he has expressed himself as opposed entirely to the view that syphilis can be transmitted to the third generation. On the opposite side may be quoted Fournier,[1] who, accepting fully the possibility of transmission to the third generation, states that the disease in this generation usually manifests itself by certain dystrophic stigmata, but that in 14 per cent. out of 116 cases observed by him, there were lesions of active syphilis in the third generation, and he adds that only three-fifths of the descendants in this generation survive to adult life.

In the records of some alleged instances of transmission of syphilis to the third generation, one source of fallacy seems to have been entirely overlooked. Inherited syphilis does not protect, at any rate permanently, from the acquired disease: numerous cases are on record in which patients with the inherited disease have in adult life acquired syphilis in the ordinary manner. Moreover, acquired syphilis, especially in women, may be latent for years, so that a woman may be ignorant of her infection until some tertiary lesion appears. It is, therefore, always possible that a parent with inherited syphilis who has syphilitic offspring may have suffered also with the acquired disease, so that the apparent transmission to the third generation may be nothing more than the ordinary transmission from parent to child.

It is obvious that great caution must be used in arriving at any conclusion upon this point; and in particular it may be said that nothing but incontrovertible symptoms of active syphilis in the offspring can be taken as evidence of transmission. To report congenital deformities of various kinds as evidence of syphilitic taint, whether in the second or in the third generation, or even to point to bossing of the forehead or a depressed bridge of the nose in an infant, is not to produce scientific evidence, for such phenomena are all common enough where there is no question of syphilis.

The possibility of transmission to the third generation must remain at present *sub judice*; this, however, is certain, that parents with inherited syphilis may have perfectly healthy children.

CHAPTER XXIII

SYMPTOMS OF CONGENITAL SYPHILIS

Symptomatology. Congenital syphilis in this country is perhaps less frequent than is generally supposed. Some statistics taken at the Hospital for Sick Children, Great Ormond Street, by the late Dr. R. J. Lee, in 1886, showed that between 250 and 300 cases of syphilis out of a total of about 12,000 out-patients were seen at this hospital each year, a proportion of 2·5 per cent. at most. My own statistics at King's College Hospital, published in 1904, showed that amongst 4,830 consecutive out-patients under the age of 10 years, there were only 29 cases of undoubted congenital syphilis, that is 0·6 per cent., and if doubtful cases were included the percentage was raised to 1·5 per cent.

Manifestations of syphilis are but rarely present at birth. According to Diday, however, 'from their very birth, and although as yet without any distinct syphilitic symptoms, the subjects of hereditary taint may often be recognized'; he describes a 'look of the little old man' as common in the new-born syphilitic child. Undoubtedly the withered, aged look to which he refers is common enough in syphilitic infants, but, so far as my own observation goes, this appearance is only gradually developed after birth, usually in association with marasmus. The infant with congenital syphilis is often a well-nourished, particularly healthy-looking infant, but so far as I have been able to ascertain by careful inquiry, there seems to be no doubt that 'snuffles' are present on the day of birth in about 14 per cent. of the cases, although there is usually nothing at the time to suggest that the snuffling is due to syphilis, as is proved by subsequent symptoms.

The date of the earliest appearance of symptoms of congenital syphilis is a matter of great practical importance in certain cases, notably where a wet nurse is to be engaged and her infant is to be examined for evidence of syphilis; at what age can we say that freedom from symptoms makes it probable that her infant is free from this disease, and that, therefore, as far as syphilis is concerned, it is safe to engage the mother as a wet-nurse? My own statistics, like those of other observers, show that the appearance of symptoms is seldom delayed beyond the end of the second month, and that it is rare for the first evidence to occur later than the end of the third month.

Date of first appearance of symptoms in 104 cases:—

In first month	54
In second month	26
In third month	16
Between end of third month and end of sixth month	3
Between end of sixth month and end of twelfth month	3
One year to eighteen months	1
Eighteen months to two years	1

These figures agree closely with Diday's statistics, collected from various observers. In 158 cases the disease showed itself—

Before the completion of one month after birth	86
Before the completion of two months	45
Before the completion of three months	15
At four months	7
At five months	1
At six months	1
At eight months	1
At one year	1
At two years	1

Whilst it is so rare for congenital syphilis to show its manifestations after the end of the first year that some authorities have doubted the diagnosis in such cases, there seems to be little doubt that the first appearance of symptoms is occasionally delayed to a much later date; for instance, I had under observation a girl in whom the first evidence of the disease, so far as could be ascertained by investigation of the past history, was interstitial keratitis at the age of seven years and five months, followed a month later by chronic effusion in both knees. To such a case the name of *Syphilis hereditaria tarda* (late hereditary syphilis) has been given. Of course it is always possible that some slight manifestation in infancy—for instance, snuffles or a rash—may have been considered to be due to more trivial causes and forgotten, but so many similar cases have been observed that the delay in appearance of symptoms is probably to be regarded as genuine.

It will be convenient first to sketch briefly the course of the disease as it is commonly seen, and then to describe in detail individual symptoms. The infant is usually healthy in appearance at birth ; within a few weeks after birth, its breathing is noticed to be snuffling, owing to some nasal coryza, and about the same time a rash appears about the buttocks and genitals, often on the face also, less commonly on the trunk and limbs. At this time the cry is hoarse, as if there were some laryngitis ; the spleen is found to be slightly enlarged, and perhaps the liver also ; the testicles may be found to be enlarged and hard ; and some loss of movement in one or more limbs may be due to syphilitic epiphysitis. The nutrition is usually affected more or less ; in some cases there is intractable wasting : the skin becomes dry and assumes an earthy yellowish-brown colour, and the face has a wrinkled, aged look. Other symptoms belonging to the first three or four months of life are iritis, choroido-retinitis, stomatitis (sometimes of condylomatous character), nephritis, and a peculiar form of inflammation of the nail matrix, causing deformity and exfoliation of the nails.

A few months later, especially if treatment has been neglected or has not been sufficiently vigorous, anaemia, sometimes very profound, is apt to occur, and the skull at this time may show definite bossy thickening of the parts adjoining the anterior fontanelle, the so-called 'Parrot's nodes' (Plate LXI) ; less commonly a thinning of the skull occurs, which may resemble the craniotabes of rickets. The hair sometimes becomes sparse, but without complete alopecia, and, if there has been severe snuffles, the bridge of the nose may assume a depressed appearance, or the whole septum of the nose may seem to sink backward, giving the nose a saddle shape.

The temporary teeth are not affected usually in appearance by congenital syphilis, but are notably prone to early decay. On the appearance of the permanent teeth, however, characteristic manifestations of the disease may be seen in the smallness and shape of the upper central incisors, which are peg shaped, that is, narrower at the cutting edge than at the base, and have the cutting edge converted into a crescentic notch, the so-called 'Hutchinsonian teeth'. (Plate LVIII.)

If the treatment has been thorough there are usually no further symptoms after those which occur during the first few months of life, but too often parents failing to realize the importance of prolonged treatment during infancy, soon weary of medical attendance and the treatment is interrupted, so that although the child may remain free from symptoms for some years these are apt to recur later, and then are of somewhat special character corresponding more or less closely with the tertiary symptoms of acquired syphilis. For instance, gummata may occur in the skin or on the bones: the palate may be more or less destroyed by gummatous ulceration; gummata may occur in the liver: a diffuse and chronic periostitis may occur, especially over the tibiae, giving rise to some thickening and deformity, and chronic affections of the joints are occasionally seen which may be of the nature of chronic synovitis with effusion, or may involve gross changes in the joint-surfaces, such as are associated with osteo-arthritis. About the age of ten years the cornea may be attacked by interstitial inflammation; and a little later the hearing may be completely lost by syphilitic affection of the internal ear. In the later years of childhood also chronic inflammation of the cerebral cortex and meninges may occur, causing slow mental deterioration, the so-called juvenile general paralysis; glandular enlargement at this time may also be due to congenital syphilis. With the exception of condylomata at the anus (Plate LVII) or in the mouth there is no tendency to recurrence of the skin eruptions of early infancy, and it is very rarely that any symptoms of active syphilis occur after the age of about sixteen years.

Such in outline is the course of congenital syphilis. It must not, of course, be supposed that any one patient is likely to suffer from all or even from the greater number of these symptoms. In many cases the symptoms are remarkably few: in some, as already mentioned, there may be no symptoms in infancy, and it is only when interstitial keratitis or some periostitis appears in later childhood that the disease becomes evident.

In inherited syphilis also, as in some other diseases, there is a striking tendency to affection of certain tissues or organs in certain families: for instance, Dr. J. Thomson[2] records a family history in which out of four children three had syphilitic epiphysitis, and another in which out of seven children four showed syphilitic disease of the fundus oculi with other symptoms. Mott[3] records the history of a family in which the father and mother had acquired syphilis, the father died of syphilitic brain disease, the mother died of some organic brain disease (nature not ascertained) one daughter and one son were imbecile, and two other daughters were 'of low type intelligence and moral instinct': he also mentions[4] a family in which out of three brothers with signs of congenital syphilis, one died with general paralysis and one was congenitally imbecile.

It remains now to describe in detail the various affections of the different organs and tissues.

Respiratory System. This may be considered first inasmuch as 'snuffles' is the earliest symptom in most cases of this disease. Rhinitis, producing snuffling respiration or 'snuffles', occurs according to my own observation in 70 per cent. of infants affected with congenital syphilis, and careful inquiry showed that in some cases it was present on the day of birth. In many cases there is very little coryza with it, but nasal respiration is obstructed so that the infant snorts in breathing, and may have some difficulty in sucking: but sometimes there is much discharge from the nares which may be simply mucus or muco-pus, or may be purulent and stained with blood. In the slighter degrees the rhinitis does not differ from that seen with simple catarrhal affection of the nasal mucosa, but ulceration of the mucosa seems to occur very rapidly in some cases and necrosis of the underlying bone or cartilage; so that slight mucous discharge passes quickly into a purulent or sanious discharge, which may, as Diday points out, contain small fragments of exfoliated bone. The following case illustrates the rapidity with which such destruction may occur: Thomas L. came under my care at the age of six weeks: snuffles had begun at five and a half weeks: he had a syphilitic rash on his face, some iritis and probably choroiditis, the spleen was enlarged and he was wasting. By the age of twelve and a half weeks the bridge of the nose had fallen in almost completely, so that had the infant lived he would have been disfigured for life by 'saddle nose'. He died, however, five weeks later. The rhinitis of congenital syphilis may give rise not only to deformity of the nose, but also to ozaena.

Very soon after the commencement of the snuffles, hoarseness of the cry is noticed which is due to laryngitis. This was present in 14 per cent. of my cases. The laryngitis of congenital syphilis is not necessarily associated with ulceration in the larynx; it may like the rhinitis consist only of inflammation with swelling of the mucosa, but resembles the disease in the nose also in a tendency to ulceration of the mucous membrane with necrosis of the underlying cartilage. In an infant who had shown marked hoarseness of cry during life and who died at the age of four months, I found at the autopsy only slight thickening and roughening of the mucosa over the arytenoid cartilages; in another who died at the age of seven months, having had during the last few weeks of life great hoarseness, I observed no naked eye lesion in the larynx. In other cases, however, gross lesions are found. Dr. Carpenter[5] records the case of an infant aged four months in whom the ary-epiglottic folds were found to be swollen and there was an ulcer perforating the thyrohyoid membrane and leading into a thin-walled cavity underneath the muscles. During life the cry had been aphonic and the breathing stridulous. The same writer mentions also a 'child aged thirteen months with chronic snuffles and extensive scarring of the mouth and chin, laryngeal whistling was audible all over the chest. She was subject to attacks of laryngeal spasm and her mother said that she had suffered from 'crowing' on and off for a long time.

The cry was not loud and noisy as with healthy vocal cords, but on the contrary dysphonic. She died suddenly, and post mortem the epiglottis and ary-epiglottic folds were much swollen. Both vocal cords were ulcerated, likewise the ventricular bands.' In a boy about fifteen years old, who looked as if he were nine years old, and showed evidence of congenital syphilis, I observed a marked respiratory obstruction from tracheal stenosis: such a condition no doubt may result from gummatous infiltration of the trachea, as in a boy aged five years described by Sharp,[6] in whom increasing difficulty of respiration with loud stridor was found to be due to a tumour in the trachea: the epiglottis and left arytenoid were thickened; the tracheal condition was diagnosed as gummatous and in forty-eight hours there was definite improvement on anti-syphilitic treatment. Laryngeal syphilis is sometimes associated with syphilis of the pharynx. Garel[7] reports the case of a girl aged nine years in whom the fauces and pharynx showed ulceration, and there was extensive infiltration of the upper part of the larynx. Such an association is, however, uncommon.

Both the soft palate and the hard are liable to destruction by gummatous infiltration and subsequent ulceration, with necrosis of bone, causing perforation. So far as my own observations go these lesions would seem to occur chiefly after the end of infancy, i.e. beyond the age of two years, and most often in late childhood. Dr. J. N. Mackenzie[8] from a study of 150 cases of throat disease due to congenital syphilis concluded that girls were more liable than boys to pharyngeal ulceration (41 girls to 28 boys).

Mr. Hutchinson has pointed out that in cases in which the palate and nose are attacked the teeth rarely show the characteristic appearances described by him.

Congenital syphilis very rarely affects the lungs. It has been customary to describe a syphilitic pneumonia in which the lung has a white hepatized appearance, the 'pneumonia alba' of Virchow. Little has been added to Dr. Greenfield's[9] description of the condition from a case which died at the age of twelve months, and which showed slight pleurisy with a firm tough lung which on section was of yellowish white colour, smooth and intersected by bands of fibrous tissue running through its substance. Microscopically it showed extreme fibrosis with much fibronuclear proliferation in the septa and walls of the alveoli. Similar cases have been described since by Symonds[10] and Carpenter.[11] It is important to note that this condition is not limited to stillborn infants or to those dying shortly after birth. Carpenter has recorded one in which death did not occur until the age of thirteen months; Greenfield's case lived till twelve months. The question arises whether this condition may not be consistent with much longer life and then give rise to the clinical signs and symptoms of chronic bronchiectasis. This at any rate may be said with certainty—that fibroid disease of one lung is by no means uncommon in children: it is easily recognizable clinically by the contraction of one side of the thorax, the signs of consolidation and of bronchiectasis and the displacement of the heart towards the affected side. In the majority of these cases there is a history of some bronchopneumonia in years gone by, especially with whooping cough or measles, but occasionally there is clear evidence of congenital syphilis in the child, or in its brothers or sisters; may not such cases be examples of chronic syphilitic pneumonia which has lasted sufficiently long to produce contraction of the lung and bronchiectasis? It might have been expected that so generalized a disease as syphilis would almost certainly affect both lungs, but in the cases which I have mentioned as occurring in early infancy the chronic pneumonia has been either limited to or has affected chiefly one lung: so that the unilateral character of the fibrosis of the lung which is seen in later childhood would not militate against a syphilitic origin.

A case recorded by Greene (quoted by Mr. Hutchinson in his work on Syphilis) strongly supports the view that pulmonary fibrosis after the period of infancy may be due, as I have suggested, to congenital syphilis. A child aged six years was found to have extensive fibroid disease of one lung and a few minute patches of fibroid induration in the other: the upper central incisors were small and peg-shaped, the spleen was enlarged with ‘ typical syphilitic thickening and puckering ’, and the capsule of the liver was thickened.

Gumma has occasionally been found in the lung as an early manifestation of congenital syphilis : I have myself seen one case showing a gumma in the lung at a few weeks old, and Behrend[12] in an infant who died with melaena neonatorum found numerous gummata in the lung with some ‘ white hepatization ’. Barlow[13] recorded the case of an infant aged four and a half months who with syphilitic disease of bones showed at the surface of one lung a small greyish yellow mass semi-gelatinous in consistency the size of a split pea, which he took to be a gumma.

The Skin, Nails, and Hair. The cutaneous eruptions of congenital syphilis will be considered first, as these with snuffles constitute in most cases the earliest manifestations of the disease. A characteristic rash was present in 69 per cent. of my cases ; in 2 per cent. a rash (pemphigus) was present at birth.

Pemphigus, which is a rare form of eruption in the syphilitic child, occurs usually at an earlier age than the other cutaneous manifestations : it is usually present at birth although it sometimes begins some days later. It is particularly liable to occur on the palms and soles and may be limited to those parts : the bullae are often of large size, as large as three-quarters to an inch in diameter, and may contain serum or turbid contents mixed with blood : usually the bulla is flaccid and soon bursts, so that by the time the rash is seen by the physician the only remains of the eruption may be patches of loosened and shrivelled epidermis only partially covering the brownish red glazed areas which were the bases of the vesicles. The pemphigus of congenital syphilis is not to be confused with the pemphigus neonatorum which begins after birth and is the result of some infection of the skin with pyogenic micro-organisms : the syphilitic variety is distinguished usually by its presence at birth and sometimes by its limitation to the palms and soles. Great stress has been laid upon the grave significance of syphilitic pemphigus; certainly it occurs chiefly in cases which suffer severely with syphilis, but it does not by any means necessarily indicate a fatal issue. The commoner eruptions of congenital syphilis which begin usually during the first two months of life may be described as erythemata, which may be diffuse or macular, desquamations, fissures, and condylomata.

The erythematous rashes affect chiefly the perineal region and the face: the distribution on the latter is peculiar; if the face be considered as divided into thirds by vertical divisions the middle third is the part specially affected by the syphilitic rash. A rash limited almost entirely to the chin, the upper lip, the inner ends of the supra-orbital ridges and just above the bridge of the nose, is strongly suggestive of syphilis. Perhaps the commonest form of eruption is the macular; reddish brown or 'raw-ham-coloured' areas, roughly round in shape, but tending to run together into irregular areas, they are little if at all raised, the surface is dry, and occasionally there is slight fine scaliness over the surface or at the edge of the maculae. The colour in some cases is yellowish brown, rather than of the more typical coppery reddish brown tint.

On the perineum and especially down the inner side of the thigh and leg to the instep there is often a diffuse erythema, having a dry glazed appearance and showing at its margin splashes as it were of erythema, detached patches which resemble the discrete maculae already described. There can be little doubt that the distribution of the rash in these parts is determined to some extent by the irritation of urine and faeces; for in cases of undoubted syphilis the area affected corresponds sometimes very closely with the 'towel-area'; and indeed this is likely enough when it is considered that the rashes of acquired syphilis in adults, for instance, the so-called 'syphilitic psoriasis' has its distribution determined very largely by the incidence of traumatism or irritation.

Desquamation is a marked feature of the rash in many cases of congenital syphilis and an extensive peeling of the palms and soles a few weeks after birth is very characteristic; the epidermis peels off in large flakes which occasionally are as much as an inch square.

Fissures or rhagades are not a very frequent manifestation:

they occur at the junctions of skin with mucous surfaces, about the mouth and anus, and are well shown in the accompanying illustration from a photograph kindly lent by Dr. John Thomson of Edinburgh (Plate LVI *a*). The fissures are sufficiently deep in some cases to cause permanent scarring, so that radiating scars are left which are pathognomonic of the disease (Plate LVI *a*). It is important to realize that it is only when the scars are definitely linear and not limited to the angles of the mouth that they can be regarded as evidence of syphilis : it is not uncommon to find some irregular scarring at the angle of the mouth in children who have suffered with any severe illness in which the sodden ulcerated condition known as ‘ perleche ’ has occurred in this position. The radiating scars of syphilis are seen in the upper lip directed upwards and outwards from the edge of the lip on each side of the median projecting portion, which itself is usually free from fissures : in the lower lip there are fissures often along the whole length of the lip, radiating downwards from its edge. Condylomata occur most often on the mucous membranes or on the skin near its junction with the mucosa ; the anus is the commonest situation, but it is not very rare to find them on the mucosa of the mouth, perhaps usually just inside the angle of the mouth. They are occasionally found also on the skin in any flexure or part where moisture or sweat may collect, for instance in the groin or axillae, and sometimes at the umbilicus. I have seen also large dry wart-like patches on the forehead evidently condylomatous, and associated with similar but moist patches on the scrotum and at the anus. The condylomata in moist situations are often in appearance very like a mass of fungating granulations (Plate LVII); the raised plaque-like patch has a greyish moist surface, and sometimes one large patch a quarter of an inch in diameter is adjoined by several smaller patches like flat-topped warts. Condylomata are sometimes found as the only evidence of syphilis at the time, but more often they are associated with other manifestations, and almost always they are followed or preceded by other evidence of the disease. I have never known condylomata to be present at birth, but I have known them to occur as early as the fourteenth day after birth, and they may be seen at any subsequent period of infancy. Whilst the other eruptions of congenital syphilis are almost limited to the first year of life, and indeed, are very rare after the age of six months, condylomata differ in their tendency to occur with almost equal frequency during infancy and at a later age unless the treatment with mercury has been very thorough: for instance, a boy aged three years was brought with a history of having had snuffles at three months, when first seen at three years he had condylomata at the anus and syphilitic glossitis, and two months later had chronic periostitis of the tibia: he had apparently had no treatment for the syphilis in infancy.

Another affection of the skin which is seen after the period when the common initial eruptions of congenital syphilis occur is that described by Sir Thomas Barlow as 'syphilitic furuncles'. I cannot do better than quote Dr. Coutts's [14] description of them. 'The furuncle', he says, 'in its typical form consists of an elevation of the epidermis of the size of half a hazel nut, the raised epidermis being generally of a deep purple colour. There is very slight hardening of the surrounding and underlying skin, and under the purple epidermis is a scanty secretion of ill-formed pus. If left to itself it may persist for long without the skin giving way, but under mercurial treatment it rapidly disappears without scarring. Without treatment it is apt to leave a small nodular thickening in the subcutaneous tissue with a corresponding slight depression in the overlying epidermis. The small nodular thickening in the subcutaneous tissue may occasionally be found preliminary to the formation of the cutaneous pustule.' Dr. Coutts says that these syphilitic furuncles are rare before the eighth or ninth month, and are probably most common in children two or three years old. They occur most often on the upper and outer part of the thighs.

There can, I think, be little doubt that some at least of these lesions described as 'syphilitic furuncles' are identical with the 'cutaneous gummata' of other writers. In my own experience such lesions have been very rare, but Dr. Carpenter,[15] amongst 364 cases showing cutaneous eruptions with congenital syphilis, found 70, that is, a little over 19 per cent., showing cutaneous gummata. 'These', he says, 'are usually the size of a pea, but now and then may reach that of a marble, a chestnut, or a walnut. They are indolent, cellular, infiltrations of the skin, which in course of time break down and discharge their purulent contents by a small round central opening.' He says they occur chiefly in the first year, and his statistics show that more than half the cases were in the first six months of life. A very rare affection of the skin in congenital syphilis is phagedaenic ulceration, which may involve not only the superficial structures, but even the deeper tissues as in the accompanying illustration (Plate LVI, Fig. *b*), for which I am indebted to Dr. John Thomson of Edinburgh; in this case the nasal cartilages have been partially destroyed as well as the overlying skin. In connexion with the skin manifestations of congenital syphilis must be mentioned two phenomena which are noticeable sometimes in infants with the disease, namely, the café-au-lait colour, and the dry papery character of the skin. There is a curious tendency to a brownish yellow tint of the skin; this is seen most often where there is considerable wasting, as happens in some cases during early infancy, but it is seen also in later infancy where there is anaemia, and the combination of this coloration with the pallor of anaemia gives rise to a very characteristic appearance, which may at once suggest syphilis. A dry papery condition of the skin, which shows fine creases, resembling those made by crumpling paper, is sometimes very noticeable, I think, chiefly in the most severe cases of syphilis with marasmus, and perhaps more on the trunk than on the limbs.

Associated usually with the early skin eruptions of congenital syphilis, there is occasionally seen a chronic affection of the nails, syphilitic onychia. The matrix undergoes inflammation, so that the nail over it becomes opaque, loses its gloss, and shows irregularities of its surface; and this process occurring chiefly near the proximal end of the nail-bed, the nail alters, and may, as Mr. Hutchinson has shown, assume an appearance as if pinched together laterally, while the distal end is of normal width; the whole nail is gradually shed, and under mercurial treatment a healthy nail takes its place. This change may occur both in the hands and in the feet. Diday quotes Guerard as having seen exfoliation occur repeatedly in one case: ‘I have seen in a new-born child affected with syphilis the nails of the hands and feet gradually become atrophied, grow longer, and narrower in appearance, and fall off at last to make way for more healthy nails, which underwent the same process, and this happened three times in succession before really sound nails remained.’ A more acute inflammation may occur, the matrix undergoing a change comparable to the pemphigus which occurs on the skin, and which indeed is sometimes associated with this nail affection, the nail is raised and loosened by a fluid exudation beneath it; this collection of sero-pus escapes by the side of the nail which is ultimately shed. These varieties of onychia occur usually during the first few months of infancy, at the time when the skin eruptions are most frequent.

The hair is affected in congenital syphilis in two ways; its growth may be excessive or it may be arrested. An unusually abundant crop of dark hair at birth or in very early infancy has been described by many writers as a symptom of congenital syphilis, and sometimes designated ‘the syphilitic mop’ or ‘wig’: the hair in these cases is not abnormal in any way except in its abundance and its rapid growth. I observed this phenomenon in 4 per cent. of my cases: it is, of course, not pathognomonic of syphilis; any infant may have a similar abundance of hair, but taken with other symptoms it may be of some value as confirmatory evidence. More characteristic is the opposite condition of alopecia; this occurred in 6 per cent. of my cases. It consists of a thinning of the hair, especially over the vertex: it never, so far as I know, leads to complete baldness, but leaves the hair so sparse that the baldness is sufficient to attract notice at once. This alopecia may occur at a later period than the initial skin eruptions; twice I have known it to begin in the second year, but more often it begins within the first six months, in one of my cases it began at the age of eight weeks; in one an unusually abundant crop of hair at birth gave way to subsequent alopecia. The alopecia may affect the eyebrows as well as the scalp, and, as Barlow has pointed out, thinning of the eyebrows by alopecia in an infant a few months old is always very suggestive of syphilis.

The Mouth and Teeth. I have already described the ulceration which occurs in the soft and hard palate in connexion with congenital syphilis, and I have mentioned the occurrence of condylomata or 'mucous patches' on the mucous membrane of the mouth. There remains to be mentioned the occurrence of stomatitis. Mr. Hutchinson has attributed the characteristic deformity of the permanent upper central incisors to the occurrence of inflammation of the gums in early infancy. Apart from the occurrence of condylomata in the mouth, it is not clear that there is any special form of stomatitis associated with congenital syphilis in infancy. I have sometimes seen a condition resembling a simple catarrhal stomatitis, the mucous membrane of the mouth is greyish white, in patches, or in streaks as if it had been rubbed with silver nitrate; the appearance differs from that of the condylomatous patch, which appears thickened and plaque-like, whereas the inflammation to which I refer is quite superficial, and the patches are not, so far as can be detected with the naked eye, raised above the level of the surrounding healthy mucosa. Possibly this superficial inflammation may be similar to that which occurs in the laryngeal mucous membrane, for this stomatitis is associated in some cases with hoarseness and aphonia. In appearance it differs in no way from the stomatitis which is often seen in infants who are entirely free from syphilitic taint.

Glossitis is not very uncommon in congenital syphilis; it was present in 4 per cent. of my cases. In some cases the epithelium of the tongue shows a patchy thickening, in others there is ulceration; both these changes have in my experience been chiefly in the middle of the dorsal surface. The patch of thickening has the appearance of a piece of wash-leather, and is slightly raised above the surrounding surface; in some cases it has the moist, sodden, whitish look of a condyloma; in others it looks dry, indolent, and yellowish-brown, as if there might be some gummatous infiltration of the superficial part of the tongue. If ulceration occurs it is superficial, with well-defined but not raised edge, and is usually oval, with its long axis corresponding with that of the tongue. Such changes are met with at any period of childhood, but most often during infancy—that is, under two years of age.

For instance, a male infant was brought at the age of five weeks for wasting; a syphilitic rash had been present since fourteen days old, snuffles began at six and a half weeks old, and when seen, at the age of eight weeks, there was a roughly oval ulcer in the mid-line of the dorsum of the tongue, which is described in my notes as 'extending forward to within half an inch of the tip of the tongue, and measuring about half an inch in length; it has a yellowish wash-leather base, and, though shallow, extends completely through the mucous membrane'; the ulcer measured about a quarter of an inch transversely. Under cutaneous inunction of mercury and a mercurial dusting powder to the rash on the buttocks, the ulcer of the tongue rapidly healed, the syphilitic rash over the rest of the body quickly disappeared, but the child wasted and died several weeks later.

An example of chronic glossitis without ulceration, and occurring unusually late, was the following: James J., aged three years, was said to have had spots on his tongue for nine weeks. He was a fat, healthy-looking boy, with red cheeks, and nothing in his appearance to suggest syphilis. The tongue showed 'very marked patchy thickening on the centre of the dorsum', as if it had been rubbed with silver nitrate; on touching the patch with the finger it felt tough and infiltrated. The nature of the glossitis was explained by examination of the anus, which showed typical condylomata. Under mercurial treatment the glossitis and the condylomata were fast disappearing a week later.

Teeth. The affection of the teeth in congenital syphilis is of great importance, for, as originally pointed out by Mr. Hutchinson, the permanent teeth may give the only conclusive evidence of the disease in an otherwise obscure case.

It is generally stated that the primary teeth show no characteristic change; this, however, is perhaps not so universal a rule as has been believed. I have elsewhere recorded a case which may be quoted in this connexion: a male infant aged fourteen months had upper central incisors resembling in every particular the so-called 'Hutchinsonian teeth'; they were of screw-driver shape, narrower at the edge than at the base; they showed at the cutting edge a well-marked shallow crescentic notch, and in addition showed that undue separation from one another which is common with the typical syphilitic incisors of the second dentition. There was no other evidence of the disease in the infant, but the family history was itself strongly suggestive: the first child had been still-born at six months, the second premature, an eight-months child which lived only nine weeks, the third (a seven-months child) was deaf and dumb, the fourth was the patient. Mr. Oakley Coles ('Trans. Odont. Soc.', vol. ix, p. 258), has recorded a case in which there were 'peg-shaped temporary teeth, which were very characteristic, occurring in a child the mother of whom had long been the subject of syphilis'. But such cases are very exceptional, and it must be admitted that, as a rule, there is nothing to suggest syphilis in the milk teeth. These, however, even though they do not show the characteristic changes which are seen in the permanent set, probably do not escape affection altogether, for it has been observed in many cases that the enamel is imperfectly formed and thin, so that these teeth are very liable to early decay. It has been stated by some writers that the eruption of the temporary teeth is retarded in congenital syphilis, but from my own observation I am more inclined to think that their eruption is hastened by this disease—certainly many syphilitic infants cut their first teeth rather before the usual time. It must be remembered that syphilis is associated with rickets in a large proportion of cases, and the effect on dentition may then be modified according to the predominating influence of either disease, the effect of rickets, of course, being to delay the eruption of the teeth.

Mr. Hutchinson[16] has described suppuration in the tooth-sacs in infants with congenital syphilis; as a result of this he says 'the crowns of the teeth, almost always the upper central incisors, are exfoliated before they are cut'. He adduces this phenomenon, which I think must be an exceedingly rare one—I have never met with an instance of it myself—as evidence that the gums and tooth-sacs are liable to congestion and inflammation in syphilitic infants, an occurrence which, it is suggested, may account for the malformation of the permanent teeth. Such an influence occurring during the first two or three months of life might well affect the permanent incisors, for these begin to be calcified one month after birth

(Magitot, quoted by Tomes). When one considers that the syphilitic infection dates possibly from the time of conception, and certainly in most cases from several months before birth, it is remarkable that the temporary teeth, which undergo the greater part of their development in the gum before birth, are so little affected.

The permanent teeth show very marked and very characteristic changes in some cases, chiefly in the upper central incisors (Plate LVIII). These are widely separated both from one another and from the lateral incisors; this separation is due, in part at least, to their abnormally small size, in consequence of which they do not fill their usual space. They are abnormal also in shape, the cutting edge is usually narrower than the base, it is rounded at its two ends instead of showing sharply angular corners, and, most characteristic of all, the edge itself is rendered concave by a crescentic notch (Plate LVIII).

These changes are usually limited to the upper central incisors, but it is not very rare to find similar but less marked changes also in the lower central incisors. Syphilitic affection of the canines is extremely rare: I am not aware that it has been recorded hitherto, but the accompanying illustration (Plate LIX), for which I am indebted to Mr. C. E. Wallis, Assistant Dental Surgeon to King's College Hospital, who showed me the case, proves that it does occur; the two upper central incisors are slightly notched, the right upper canine shows well-marked notching, which in Mr. Wallis's opinion was similar in origin to the much commoner notching of incisors in congenital syphilis. The molars show changes which are less well-defined: they have a 'dome-shaped' appearance, owing to the poor development of their cusps and the rounding off of their angles. None of these changes are necessarily present; indeed, judging from my own experience, I should say that it is quite a small minority of children with congenital syphilis who show the typical notched incisor or indeed any condition of the teeth which can be referred with certainty to the syphilis.

Eyes.[*] Affections of the eye are very common in congenital syphilis. I found that out of sixty infants under the age of one year, nine showed either choroiditis or iritis, or both these lesions, whilst including children up to the age of twelve years, out of 100 consecutive cases of congenital syphilis at least 23 per cent. showed syphilitic disease of the eye, and the percentage would probably have been higher had an ophthalmoscopic examination been made in all cases, for there may be extensive syphilitic disease of the fundus without any symptoms to suggest the need for ophthalmoscopic examination.

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[*] For special account see Vol. IV.

Some of these ocular changes must be reckoned amongst the earliest manifestations of congenital syphilis. Syphilitic changes in the fundus oculi certainly occur very soon after birth, and it seems likely that they may be congenital, for choroiditis, apparently of considerable duration, is found in some syphilitic infants at a very early age. In an infant aged twelve weeks, who had been born with pemphigus, whose father acknowledged having had syphilis, and whose mother had also been under treatment for symptoms which were almost certainly secondary syphilis, there was marked retino-choroiditis and there were also opacities in the vitreous and evidence of past iritis in posterior synechiae. In another infant, aged six weeks, who had snuffles and a syphilitic rash, there was iritis, and my colleague, Mr. Cargill, the ophthalmic surgeon, thought probably also some choroiditis.

The appearances in the choroid are usually irregular white patches with dark irregular borders of pigment, and sometimes dark spots or patches of pigment without an adjoining white patch, scattered about other parts of the fundus. There are cases in which, without any white areas at any part, there are numerous small collections of dots or streaks of black pigment, and, as Mr. Hutchinson has pointed out, the disease in these cases may begin peripherally, and the pigment patches may be arranged in the form of a zone. Choroiditis or choroido-retinitis may interfere greatly with vision, but, on the other hand, it is astonishing how extensive the patches of choroidal atrophy may be without producing any great defect of vision. Often nystagmus results from this affection of the eye, and I think that it would be correct to say that when nystagmus is present in a child with congenital syphilis it nearly always indicates the presence of choroiditis. Choroiditis is associated in many cases with opacities of the vitreous, and these also occur at a very early age, as, for instance, in the case mentioned above, where they were present at the age of twelve weeks.

Both choroiditis and vitreous opacities are found with special frequency in children who show affections of the brain in congenital syphilis. I shall describe the nervous disorders associated with this disease later, but here it may be said that idiocy, the mental degeneration of general paralysis, hydrocephalus, and some cases of spastic paralysis in syphilitic children are frequently associated with choroiditis or choroido-retinitis and opacities in the vitreous.

Iritis I have mentioned also as occurring during the first few months of infancy; Mr. Hutchinson[17] has summarized the clinical phenomena of this affection so admirably that I cannot do better than quote the aphorisms in which he embodies his conclusions: 'The subjects of infantile iritis are much more frequently of the female than the male sex; the age of five months is the period of life at or about which syphilitic infants are most liable to suffer from iritis; syphilitic iritis in infants is often bilateral, but quite as frequently not so; iritis as it occurs in infants is seldom complicated, and is attended by but few of the more severe symptoms which characterize the disease in the adult; notwithstanding the ill-characterized phenomena of acute inflammation, the effusion of lymph is usually very free and the danger of occlusion of the pupil great: mercurial treatment is most signally efficacious in curing the disease, and, if present, in procuring the complete absorption of the effused lymph; mercurial treatment previously adopted does not prevent the occurrence of this form of iritis; the subjects of infantile iritis, though often puny and cachectic, are also often apparently in good condition; infants suffering from iritis almost always show one or other of the well-recognized symptoms of hereditary taint; most of those who suffer from syphilitic iritis are infants born within a short period of the date of the primary disease in their parents.

Much later than the affections mentioned comes the interstitial keratitis of congenital syphilis. This begins usually between the ages of six and twelve years, and occurs usually in one eye before the other. The cornea first becomes hazy in the centre, then spots of more marked opacity appear in the haze and soon coalesce; these opaque patches are evidently deep in the cornea, not on the surface. Soon after the steaminess of the cornea has first appeared the conjunctiva, the sclerotic, and the cornea itself show abundant fine blood-vessels ramifying over the surface and passing deeply into the cornea. I have seen the disease occur in the other eye as early as a week after the first had been attacked, but more often there is an interval of several weeks, sometimes of several months, before the second eye is affected. Interstitial keratitis is very slow in its subsidence; a year or even longer may elapse before the treatment can be discontinued, and during the height of the affection sight may be almost completely lost; but even in the very severe cases the opacity diminishes under treatment to a surprising extent, and in the milder cases completely disappears. It has been noted by several observers[18] that interstitial keratitis sometimes relapses even after an interval of years; one writer (Hirschberg) has stated that 3 per cent. relapse owing to insufficient treatment; V. Heppel found that five out of sixteen relapsed after intervals varying from two months to nine years, while another observer (Collomb) found that nine out of 170 cases relapsed after periods varying from eight months up to fifteen years.

As some of the earlier eye affections of congenital syphilis show a special tendency to association with nervous affections, so I think interstitial keratitis is associated with special frequency with the bone and joint affections of the later stage of the disease. Mr. Hutchinson[19] points out also that this form of keratitis is seldom seen without the characteristic notched teeth.

Ears. In infancy there is no affection of the ears specially due to congenital syphilis, but, as might be expected with a catarrhal condition such as is present during the snuffles of syphilis, there may be a simple otitis media and resulting otorrhoea. At a later period, however, usually some years later than the interstitial keratitis, perhaps most often between the ages of fifteen and twenty years, a characteristic affection of the auditory apparatus occurs, namely, an insidious inflammation of the internal ear—if indeed this be the correct explanation of this obscure lesion—causing very rapid loss of hearing without pain or any external evidence of disease. In some cases there is complaint of noises in the head, but more often the only symptom is the rapidly increasing deafness, which in a few weeks amounts to complete loss of hearing.

Visceral Affections. The viscus which is most often affected by this disease is the spleen. Coutts, in 100 cases, found the spleen enlarged in sixty-two, whilst its size was probably above the normal in nineteen others. I found the spleen easily palpable in 45 per cent. of my cases, and at least one inch below the costal margin in 22 per cent. It is quite clear that absence of enlargement of the spleen cannot weigh much against a diagnosis of syphilis, but in connexion with other symptoms its presence is of some confirmatory value. Coutts points out that although the spleen is found enlarged in syphilitic foetuses—according to one observer[20] in about 78 per cent. of macerated syphilitic foetuses—it is certainly not always a congenital enlargement. The spleen is very rarely greatly enlarged in inherited syphilis, unless the so-called splenic anaemia of infants, in which there is enormous enlargement of the spleen, is to be attributed to syphilis ; in that disease undoubtedly it is common to find the bossing of the skull which was described by Parrot as syphilitic, and proliferation of fibrous tissue in the liver has been found therewith ; but it is very doubtful whether such cases are necessarily due to syphilis, even though it may be admitted that in some of them there seems to be a combination of syphilis with rickets.

The affection of the spleen in inherited syphilis is apparently usually a hyperplasia, sometimes with some degree of fibrous induration, and often with some capsulitis ; gumma, however, is extremely rare ; two cases of gumma of the spleen, one in a boy aged eleven years, and another in a boy aged six years, were recorded by myself,[21] and four others in children at ages varying from ‘ a few days old ’ up to seven years have been recorded by continental writers. Lardaceous disease is an exceedingly rare cause of enlargement of the spleen in inherited syphilis; it was present in one of the cases which have just been mentioned, with gumma of the spleen.

Liver. The liver is affected in two ways in congenital syphilis; there may be a diffuse inflammatory infiltration of the liver giving rise to cirrhosis, or there may be isolated foci of cell-proliferation producing gummata. Affections of the liver are not, however, very common as a clinical manifestation of congenital syphilis. The observations of Mervis suggest that in the most severe cases of syphilis in which the infant dies in utero, the liver is affected much more often than it is in extra-uterine life ; he found that of ninety-two syphilitic foetuses which had died in utero the liver was diseased in fifty-six. In my own series of 100 cases of congenital syphilis, not including still-born children, there were at least six who had cirrhosis or gumma of the liver; in five of these the liver condition was diagnosed during life, in one it was not recognized until after death. These figures, however, by no means indicate the frequency of liver affection, for it is often impossible to recognize cirrhosis or hepatic gumma clinically in a syphilitic infant, and even at autopsy, unless microscopic examination be made, it may be impossible to detect a cirrhosis. The researches of Gubler [22] have shown that the liver may become cirrhotic before birth, for such a change has been observed by him in syphilitic foetuses. From the fact that the cirrhosis of inherited syphilis is most often observed in infants who die during the first few months of life, and that the change in the liver in these cases is already of a fibrous or fibro-cellular character, it seems probable that the cirrhosis of inherited syphilis is commonly of antenatal origin. The cirrhosis is accompanied usually with some enlargement of the liver, not very great as a rule but sufficient to be noticeable during life as well as after death. The liver may feel firmer than normal, but even at autopsy the alteration of consistence is sometimes so slight as to be doubtful, although the microscope proves that there is very definite cirrhosis ; so that undue hardness of the liver must not be looked for as essential to the diagnosis of cirrhosis. The surface is usually smooth, and clinically there is no tenderness ; jaundice is present in some cases, and more rarely ascites. As an instance of the latter, I may mention the case of a male infant who came under my care at the age of three and a half months; he had then had snuffles for two weeks, and had upon the trunk and legs brownish stains left by a recent rash, presumably of syphilitic character. Both the spleen and the liver were much enlarged. The infant was anaemic, and there was slight general oedema. Family history showed first two miscarriages, then an infant who had snuffles, and wasted and died when he was a year old, then the patient. The infant died four days after I saw it. Post mortem there was considerable ascites, the liver showed cirrhosis, and some pale yellowish patches about the size of a sixpence on section, some on the surface, some in its substance.

The cirrhosis in these cases consists of a diffuse interstitial hepatitis, extending more or less evenly throughout all parts of the liver and particularly between the liver-cells so that individual cells or groups of two or three cells are surrounded by the newly-formed fibrous tissue, and in many parts undergo atrophy; but the change is, on the whole, so uniform that the surface of the liver remains quite smooth and regular. The cirrhosis is therefore an intercellular cirrhosis, differing both in its microscopic and in its macroscopic appearances from the multilobular cirrhosis which is met with occasionally in later childhood, giving rise to a 'hobnail' contracted irregular liver, in most cases without apparent explanation. Is there any connexion between these two conditions? As I have already mentioned, intercellular cirrhosis seems to be associated usually with a severe incidence of syphilis, so that if the infant is born alive he is not likely to survive beyond the period of infancy, indeed rarely lives longer than a few months; but, on the other hand, cases are occasionally met with in which an exactly similar condition is found at the age of two or three years, and it seems possible that if life were prolonged for several years, contraction of the newly-formed fibrous tissue, possibly with some regeneration of liver-cells, might give rise to the contracted 'hobnailed' liver. But although such a sequence seems possible, I know of no facts to prove that it occurs. In the Museum of the Hospital for Sick Children, Great Ormond Street (Catalog. Spec., 493), there is the liver of a boy aged ten years and four months showing cirrhosis. The boy had jaundice and much ascites on admission; he had 'Hutchinsonian' teeth, syphilitic retinitis, a sunken nose, and scarring around the mouth. The liver was felt two fingers' breadth below the costal margin, and was hard and smooth; the spleen also was enlarged. An autopsy showed that the liver was unduly firm and greatly enlarged, but smooth on the surface. On section it showed a mottled appearance, due to alternating grey and brownish-red areas; microscopically the capsule was seen to be thickened; there was only slight increase of fibrous tissue in the liver, the cells of which were much atrophied; the boy had also gummatous meningitis with syphilitic arteritis, and some early interstitial nephritis. This case, at any rate, shows that cirrhosis in late childhood may be syphilitic, but the condition found was not the contracted 'hobnailed' liver which, as I have several times observed, occurs in later childhood without any history of the alcoholism of which a similar liver in an adult would be considered almost conclusive proof. It is easy to ascribe such cirrhosis in childhood loosely to syphilis, but facts are needed to prove this relation, and if it be proved, it has still to be determined whether the cirrhosis in these cases is a later stage of the uniform intercellular cirrhosis of infancy or whether it has commenced at a much later period of childhood as a multilobular cirrhosis.

In addition to the syphilitic hepatitis or cirrhosis there is found in the liver a gummatous condition, which in the foetus and in early infancy rarely results in the production of a large mass, but takes the form of small greyish-white or yellow nodules, varying in size from that of an ordinary pin's head up to that of a cherry-stone. They are roughly circular in shape, but not encapsuled, and may be either on the surface or in the substance of the liver. These minute gummata are of no clinical importance, for they are only recognizable post mortem. They may be associated with diffuse intercellular cirrhosis.

In later childhood gummata occur in the liver, forming palpable bosses on the surface of the organ, and by their association with other late manifestations of congenital syphilis are readily recognized during life; for instance, a boy aged six years, whose birth followed three successive miscarriages, and who had shown a rash and snuffles soon after birth, had the remains of former iritis and a gumma over one ulna when he was admitted into hospital, with a smooth rounded boss projecting palpably from the right lobe of the liver. Under anti-syphilitic treatment the projecting tumours rapidly disappeared, leaving only some slight irregularity of the surface of the liver. Dr. H. Ashby[23] has recorded the case of a girl, aged ten years, who had been under observation four or five years with syphilitic periostitis of the bones of the forearm and tibiae. An autopsy showed fifteen or sixteen gummata in the liver, some projecting on the surface, some in its substance. Those visible on the surface were 'the size of small nuts'. In this case the liver was extremely lardaceous, as were also the spleen and kidneys. Dr. Coutts[24] mentions two children, eight or nine years old, with a clear history of inherited syphilis, in whom there was ascites with enlargement of the liver, and what were taken to be gummata could be felt on the surface of the liver. Both recovered under anti-syphilitic treatment. The good results in these two cases, as in the one described from my own observation above, and in another which I saw at the age of six years (a male) with interstitial keratitis and syphilitic periostitis, and with an enlarged liver with projecting bosses on its surface, show that the occurrence of gummata in the liver is by no means necessarily of sinister prognosis. No doubt the absorption of the gumma under treatment is not so complete as to leave no scarring behind: in one case which I observed for several years after the gumma had subsided there remained a palpable irregularity of the surface of the liver, although the rounded swelling of the gumma had disappeared rapidly under treatment.

Kidneys. It has been shown in recent years that congenital syphilis may cause inflammatory changes in the kidneys. In 1880 Coupland[25] recorded two cases of parenchymatous nephritis in girls respectively of thirteen and eighteen years with inherited syphilis. In 1894 Massalongo[26] reported the case of an infant aged eight months who had chronic interstitial nephritis with other evidence of syphilis. A boy aged six years died in the

Hospital for Sick Children, Great Ormond Street, under the care of Dr. C. West, with a definite history of congenital syphilis. At the autopsy it was found that the spleen was enlarged and contained numerous gummata varying in size from 'a pin's head to a horse-bean'; there was gummatous deposit in the liver and some interstitial nephritis. Carpenter,[27] in 1901, published a full account of a case of acute nephritis in a syphilitic infant aged five weeks. There was general oedema, the urine was albuminous and contained hyaline, epithelial, and blood casts. The kidneys post mortem did not reveal any obvious naked-eye alteration, but on microscopic examination there was found to be a patchy nephritis both parenchymatous and interstitial. The same writer [28] has published another case in an infant aged five months. The date of onset of the disease was not clear, but apparently albuminuria was present a month before death. The changes in the kidney were found to be parenchymatous only; there was no interstitial change, but the walls of the blood-vessels were thickened apparently by a mesarteritis. Sutherland and Walker [29] have recorded the case of an infant aged sixteen months who died with cerebral symptoms due to syphilitic arteritis, in whom the kidney showed acute nephritis, chiefly interstitial; and also another case which died at the age of eight months with similar acute interstitial nephritis. I have had three cases under my own care, one of which developed general oedema at the age of six weeks, and died six weeks later. Autopsy showed acute nephritis. Another had ascites with symptoms of nephritis at the age of three years and three months, and showed post mortem intercellular cirrhosis with acute nephritis chiefly of interstitial character. The third, a female infant aged three months, had pseudo-paralysis of one arm, with enlarged spleen, yellowish anaemia, and some dropsy. The urine contained a large amount of albumen. Under mercury the child rapidly recovered the use of the arm, but died shortly afterwards with a suppurative meningitis. At autopsy the kidney showed acute parenchymatous nephritis.

Of the eleven cases collected here, it will be seen that the earliest was at the age of five weeks, the oldest at eighteen years, and that while in some cases there was parenchymatous change, in others (five out of ten in which this point was noted) the change was interstitial chiefly or entirely. It is noteworthy that the symptoms dated in some cases from as early as five or six weeks after birth, a fact which suggests the possibility that nephritis may even be of intra-uterine origin. Dr. Ashby has observed a case of acute nephritis, at the age of twenty-one days, where the kidney showed a mixture of parenchymatous and interstitial nephritis suggestive of a longer duration than three weeks, but in this case there was no evidence of syphilis. Hecker[30] has found that in the syphilitic foetus there are sometimes present changes in the kidney, including proliferation of the interstitial connective tissue, but parenchymatous lesions are rarely found.

An interesting question which arises in connexion with the nephritis of inherited syphilis is its relation to the chronic interstitial nephritis which is occasionally found in children and young adults without explanation. It has been suggested that these cases may be due to inherited syphilis, but at present, beyond the presumption that such changes as have been found in the infantile cases mentioned would pass into a condition of chronic interstitial nephritis if the child survived, there is little ground for any conclusion. Dr. Sawyer[31] has published two cases which may possibly be of this nature: a boy who died at the age of four years with chronic interstitial nephritis; his father was thought to have had syphilis, but the child showed no evidence of syphilis. Moreover the pelves of the kidneys were dilated, so that the nephritis may have been secondary to the dilatation following on some past obstruction. The other case was a girl aged eighteen years, who, with chronic interstitial nephritis, showed gummata in the liver and spleen, but there was no clear evidence that the syphilis was inherited.

Haemoglobinuria. There can be no doubt that paroxysmal haemoglobinuria in children usually, if not always, indicates parental syphilis. I have notes of four cases in all of which there was evidence of syphilis either in the children or in the parents. The earliest age at which the haemoglobinuria was known to have begun was two years and eight months. All the cases were between six and nine years of age when they came under observation. Dr. Guthrie[32] has seen two sisters with paroxysmal haemoglobinuria; both had congenital syphilis. He also mentions two cases recorded by Taylor and Carpenter, in both of which there was syphilis in the family. The urine in these cases is brown or red, as if with blood, but on microscopic examination no blood corpuscles, or only very few and quite too few to account for the colour of the urine, are found; with the spectroscope the characteristic bands of methaemoglobin are seen. This coloration of the urine occurs only occasionally, and is noticeably related to exposure to cold. It is well known that in adults Raynaud's disease is closely connected with haemoglobinuria. I have not observed this association in any cases of haemoglobinuria in children, but I have recently had under my care a girl aged four years, whose fingers and toes became 'blue-black' occasionally with cyanosis. Both the mother and father had had syphilis, and the child herself had syphilitic periostitis of the tibiae. Morison[33] has recorded a case of Raynaud's disease in a boy aged eight years, in whom a history of snuffles during infancy and the history of previous still-births and a premature child were thought to point to congenital syphilis.

Testicle. Orchitis is not a very uncommon result of congenital syphilis. According to Henoch, Déprès[34] was the first to describe this condition in a report of three cases in children at ages from seven months to three years; in one of these there was some epididymitis in addition to orchitis. It occurs usually within the first five months of life; but Carpenter mentions having seen it once in a boy of twelve years, and refers to a case of Fournier's at the age of twenty-four years. Henoch[35] mentions that twelve cases had come under his own observation; the youngest was three months old, the oldest was two and a half years. He notes the distribution in ten cases: both testicles were affected in four, the left alone in four, and the right alone in two. In one case in which the testicles had remained enlarged, in spite of mercurial treatment, part of the epididymis was enlarged as well as the testis. Orchitis was present in five out of sixty-four male cases under my own observation. In three it occurred at the age of twelve weeks, in one at four and a half months, in one at twelve months. In none was it associated with hydrocele, and although I believe I have once seen a hydrocele associated with congenital syphilis, but without orchitis, I should say that hydrocele very rarely results from the inherited disease. On the other hand, Carpenter states that hydrocele is the most common complication of syphilitic affection of the testicles ; he says that it is usually not large in amount, and may be unilateral or bilateral ; he quotes Seringe as finding that hydrocele occurs in one quarter of the cases in which the testicle is affected by inherited syphilis. In the five cases to which I have referred the orchitis was bilateral in all : the testis was much enlarged (two or three times the normal size), very hard and very little tender ; in one only was the epididymis involved as well as the testis. In all these cases there seems to be a general inflammation of the testis, which is enlarged and hardened uniformly ; but localised gumma has been observed, e.g. in an infant aged nine weeks, who had a large broken-down gumma in the epididymis (Abbott, quoted by Carpenter). The occurrence of syphilitic orchitis is noteworthy for two practical reasons: first, because occurring, as it often does, in an infant under five months of age, it is a valuable help in diagnosis, being almost the only cause of enlargement and hardening of the testis at this age; tuberculosis is very rare under the age of five months, moreover it tends to affect the epididymis first and chiefly, so that it should not be confounded with syphilis; but at a later age the diagnosis may be difficult and depend largely on the associated symptoms; secondly, because if the nature of the orchitis is recognized and anti-syphilitic treatment promptly used, the inflammation speedily subsides and the organ may retain its function, loss of which would almost certainly result if the orchitis persisted owing to lack of the specific treatment.

Thymus. Diday describes suppuration of the thymus gland as a manifestation of congenital syphilis, but he adds no observation of his own to those of Dubois, who in 1850 stated that in infants who had died with syphilis the thymus on squeezing after incision yielded a few drops of pus : in a case mentioned by

Depaul a small cavity in the gland contained the pus, but in the other cases the pus seemed to be diffused through the organ. Modern investigators have failed to substantiate these findings, and it seems probable that normal appearances were mistaken for pathological conditions. So far as my own experience goes I have in a considerable number of autopsies on syphilitic children seen nothing to suggest affection of the thymus.

Pancreas. It has been stated that the pancreas undergoes an interstitial fibrosis in congenital syphilis. Dr. Rolleston has recently recorded such a case in a female infant aged three months (see Plate LXIII). I have not seen such a change myself; but Heubner[36] records the case of a child aged three and a half years who suffered for several months before death with jaundice and ascites. Post-mortem: a hypertrophic cirrhosis of the liver was found and the pancreas was enlarged to about twice its normal size; the enlargement was due to an extensive small cell infiltration about the acini, with some localised collection of cells forming little tumours about the size of a pea. No symptoms, however, have been attributed to syphilitic affection of this organ.

Lymphatic Glands. These certainly do not escape affection in congenital syphilis, although most writers scarcely allude to any change in them. I had under my care a boy, aged six years, who for several years suffered with various syphilitic affections, including gummata, in various parts, syphilitic iritis, and syphilitic joint affection. He reappeared at hospital on one occasion with a large nodular tumour in one groin, obviously, so it was thought, greatly enlarged glands; under anti-syphilitic treatment these all rapidly subsided. Hutchinson refers to a girl aged fifteen years, with interstitial keratitis, whose cervical glands became greatly enlarged; the enlargement disappeared quickly under treatment with potassium iodide. Holt states that in his experience this adenitis is usually a late manifestation of syphilis.

The Nervous System. The nervous system is affected not very rarely by congenital syphilis: in my own series ten per cent. showed cerebral affections of one kind or another. Most frequent are mental affections, either congenital or acquired; meningitis and gummatous affections occur more rarely; hydrocephalus, spastic palsies, and epilepsy are all occasional results.

Mental Affections. Amongst 142 consecutive cases of congenital syphilis I found six idiots, not including under this head cases of mental degeneration beginning after infancy, and I do not think that this gives a sufficiently high estimate of the proportion in which idiocy results from this disease, for many infants with severe syphilis die so young that it is impossible to be sure whether they are idiotic or not, and in some cases which have not been included amongst the idiotic it was thought that the infant would have proved idiotic if it had lived. I would add that in taking the histories of syphilitic children it is sometimes noticeable that there are children in the family who are mentally deficient, although they may show no evidence of the disease otherwise; for instance, I saw the third child in a family with interstitial keratitis, Hutchinsonian teeth, and scars of fissures on the lips; I did not see the fourth and fifth children, but the sixth was feeble-minded and the seventh had pulmonary fibrosis. In taking the family history of idiots there is sometimes a history very suggestive of syphilis, although there may be no means of absolutely proving it, either in the family or in the patient, e.g. Minnie T., aged fifteen months, is completely fatuous, an idiot of the 'genetous' class; the family record is: (i) a child aged thirteen healthy; (ii), (iii), (iv) miscarriages; (v) still-born; (vi) living, aged four years, said to be healthy; (vii) patient. It must be remembered, also, that there may be no evidence in an idiot of syphilis unless the fundus oculi be examined, when a choroiditis may be found, which is almost conclusive evidence of syphilis. It may be that syphilis is only an indirect factor in some cases, and that, like any other cause of ill-health in the mother, it interferes with her reproductive power, and so causes imperfect cerebral development in the foetus without producing in the foetal tissues or in extra-uterine life any of the specific lesions of syphilis. However this may be, it may, I think, fairly be assumed that parental syphilis may be responsible for congenital idiocy when there are no signs of syphilis in the child as well as in the cases where there are characteristic manifestations of the inherited disease. With regard to statistics which have been collected from idiot asylums, for instance those of Shuttleworth and Beach, who put the proportion due to syphilis at 1·17 per cent., or those of Dr. Telford Smith[37] who found only eight cases with marked evidence of inherited syphilis amongst 580 inmates of the Royal Albert Asylum, or those of Tredgold,[38] who, examining 150 cases, found definite evidence of the inherited disease in 2·5 per cent. and possible evidence in 3 per cent., it seems probable that they considerably under-estimate the effect of congenital syphilis in producing idiocy, for very many idiots do not live long enough to reach asylums, where they are seldom admitted until they are at least seven years old. Moreover, any one who sees large numbers of children in the out-patient departments of a children's hospital knows how completely the symptoms of infantile syphilis disappear in most cases, and how difficult it would be to prove the existence of syphilis in many of these children if they were seen first when they were six or seven years old. My own statistics, showing idiocy in 4·2 per cent. of cases of undoubted syphilis, suggest that idiocy is perhaps a commoner result of this disease than is generally recognized ; but this percentage cannot, of course, be compared with the statistics mentioned above, which refer to an entirely different proposition, namely, the relative frequency of syphilis compared with other causes of idiocy.

As to the *modus operandi* by which inherited syphilis produces congenital idiocy, more observations of the morbid anatomy of these cases is needed before any satisfactory account can be given. It may be suggested tentatively that in these cases syphilis may act in two ways, either by interfering with the development of the brain or by causing disease of the brain during its development. Ballantyne states that in foetal syphilis the morbid alterations in the nervous system are malformations or dystrophies, rather than diseases, for the brain, even at the end of the foetal period, is still in a state of incomplete development, and 'peccant matters acting upon it will therefore determine anomalies of construction rather than diseases in the strict sense of the word'. If this be so, it might be expected that idiocy caused by syphilis would not necessarily differ either in its clinical character or in its morbid anatomy from that due to any other condition—for instance, alcoholism or exhaustion in the mother, which also interfere with the development of the foetal brain. Some confirmation of this may be afforded by the occasional association of Mongolian imbecility with undoubted congenital syphilis in the infant, whereas it is quite certain that Mongolian imbecility is usually quite independent of this disease. But there are other cases in which it is clear that idiocy has been produced by syphilitic disease of the brain at some stage of its development. Dr. Ashby[39] has recorded a case of microcephaly in which the brain weighed three and a quarter ounces (after having been in weak spirit); the child suffered with frequent fits from the age of two months and died at the age of five months. The brain showed sclerosis and atrophy of parts of the cortex; the pia mater was unduly opaque in some parts; there had also been some inflammation of the choroid plexus and some internal hydrocephalus.

Sir T. Barlow has recorded a case in which old thickening and calcification of the pia mater was found with arteritis and choroiditis in a syphilitic infant aged ten months; it was quite clear that the condition in the pia mater was of old standing, and even assuming, as Barlow did, that the change was of extra-uterine origin, it must have dated from very early life; such a case shows that there is ample possibility for morbid changes in the brain as a direct result of syphilis, and there can be little doubt that idiocy might result therefrom.

Mental degeneration, as an acquired condition beginning after some years of apparently normal mental power, is sometimes a direct result of congenital syphilis; and if such cases were included under the head of 'idiocy' the proportion of cases of idiocy due to syphilis would be considerably higher; amongst the 142 cases of syphilis there were four such cases of mental degeneration in later childhood, which, with the six congenital idiots mentioned, would make the proportion of cases of mental defect amongst syphilitic children seven per cent.

The usual history in these cases is that the child, after being apparently of normal intelligence, at some age between five and fifteen years began to grow dull and fatuous, perhaps fat and gross. There may be occasional convulsive attacks and perhaps headaches, the pupils are usually unequal, there may be some tremor of the limbs; the knee-jerks are commonly exaggerated, but in some cases have been absent, and there may be extensor reflex of the toes instead of the normal flexion ('Babinski's sign'): in twenty-two cases Dr. Mott [40] observed in all except one progressive weakness, and in quite half the cases paralysis and contracture of the lower limbs, speech became very indistinct, and often there was difficulty in swallowing. Finally the patient becomes bedridden, probably more or less rigid in the limbs, and emaciation, with bedsores and exhaustion, ends the scene, perhaps three or four years after the first onset of mental symptoms. Such cases have been described as 'juvenile general paralysis'. Dr. Mott notes that the chief difference between the juvenile form and the disease of adults (by 'juvenile' he means, apparently, beginning under about twenty-four years of age) is the mildness of convulsions, when they occur, and the comparative infrequence of delusions of grandeur. I know not whether it be a chance association, but in all the four cases under my own observation there was chronic syphilitic periostitis of one or both tibiae, and in a case recorded by Drs. J. Thomson and Walker [41] the same association was noticed. The course of these cases of so-called 'general paralysis' in children extends over some years, perhaps four or five, or even longer; but, however slow it may be, the course seems to be always progressively from bad to worse. The lesions found in the brain are well described by Thomson and Walker, and consist of inflammatory thickening of the dura and pia mater with some adhesions, atrophy of parts of the cortex and some sclerosis, and generally dilatation of the ventricles. Similar pathological changes are met with in cases which run a much more acute course. For instance, Wilfrid S., aged ten years and eleven months, was born with pemphigus; the details of his infancy otherwise were unknown. Later he had interstitial keratitis; ten days before admission to hospital, under the care of Dr. Lees, he had severe frontal headache and vomited. Five days later he had a fit, and another on the day of admission. He died three days after coming into the hospital.

The pia mater was thickened, grey, fibrous, and opaque over the left side of the vertex of the brain, and also about the quadrate space and the Sylvian fissures at the base; there was some sclerosis and wasting of one convolution in the right frontal region. The pia mater down the posterior surface of the cord was somewhat thickened. There was no exudation of lymph; in fact none of the ordinary appearances of acute meningitis. A boy aged twelve months, who had had snuffles at the age of five weeks, with severe ‘ thrush ’, and subsequently some rash about the buttocks, and whose eyes showed retino-choroiditis and opacities of the vitreous, was admitted to hospital for convulsions with rigidity and wasting: he died after seven weeks’ illness. I found the dura mater adherent to the pia mater chiefly at the vertex, with small haemorrhages on the inner side of the dura, which was much thickened; the pia was slightly thickened, especially in the neighbourhood of the blood-vessels on the surface of the brain; the convolutions showed a dirty yellowish coloration and were hard, and in places shrunken; the cerebellum was normal. Dr. Ashby has recorded a very similar case: an infant who had suffered with syphilitic rash and epiphysitis at three months old had convulsions at the age of eight months; later some retraction of the head and rigidity of limbs appeared, and the infant became completely idiotic and died at the age of fourteen months. The pia mater was found to be opaque and thickened, especially over the vertex, but there was no lymph anywhere. The cortex was found to be softened, the cells of the grey matter were degenerated, and there was some endarteritis of the small arteries passing from the pia into the cortex.

It seems clear that in such cases there is a subacute or chronic meningo-encephalitis, and that the naked-eye changes, at any rate, differ in no way from those found in the cases described as ‘ general paralysis of the insane ’ in children.

Tabes dorsalis or locomotor ataxy has been observed sometimes in children, more often in early adult life, as a result of congenital syphilis, and in some cases has been associated with general paralysis. Dr. J. Taylor[42] mentions the case of a youth of seventeen years who had commencing optic atrophy and sluggish knee-jerks which soon disappeared altogether. He became blind, and then developed mental symptoms which necessitated his removal to an asylum. He had no signs of congenital syphilis, but his sister had characteristic signs of this disease. Taylor refers to Strümpell's case of juvenile tabes dorsalis, with symptoms, also, of general paralysis, in a girl of thirteen years, whose father had the secondary symptoms of acquired syphilis two years before the patient's birth. Dr. Taylor states that tabes dorsalis may occur as early as eight years of age, but it is certainly very rare. I have seen only one instance myself, and that not in my own practice: a boy aged about fourteen years, who had optic atrophy and the characteristic symptoms of locomotor ataxy.

Congenital syphilis seems to play a part also in the production of the spastic palsies of childhood, both of cerebral and of spinal origin. Osler, in 180 cases of infantile hemiplegia, noted one case of congenital syphilis. Sachs and Petersen noted two cases of syphilis amongst eighty-three of infantile hemiplegia, and Hadden noted two as certainly and eleven as possibly syphilitic amongst twenty-five cases of infantile hemiplegia. Amongst fifty-one cases of infantile hemiplegia under my own observation, none showed evidence of syphilis, but in two the relation of miscarriages to the birth of the infant raised a strong suspicion of syphilis. Mr. Hutchinson[43] records the case of a girl, aged five years, of feeble intellect, who showed choroido-retinitis and had left hemiplegia, with some weakness also of the right leg, beginning at three years of age. He refers also to a family, whose history Dr. Hughlings Jackson recorded, in which four out of five children showed evidence of congenital syphilis, and one of these, in addition, had right hemiplegia, with some weakness of the left leg also, while another of the four was blind, idiotic, and paraplegic. In one case under my own observation a girl aged five years, who showed mental degeneration and had previously suffered with iritis, and had some choroiditis and opacities in the vitreous, became gradually spastic in the legs. I have seen also spastic diplegia in a boy aged seven years, who was idiotic, associated with disseminated choroiditis, which made it almost certain that he was syphilitic.

In view of the cases of chronic meningo-encephalitis to which I have already referred, it might be supposed that a localised lesion of this kind might account for some of the spastic paralyses which have been observed in congenital syphilis; there is, however, very little record of post-mortem observation, and from the records of some cases it seems probable that the symptoms may sometimes be due rather to vascular lesions than to any meningeal affection; for example, in the observations of Sutherland and Walker, to which I have already referred, rigidity of limbs and paralysis in a syphilitic girl aged ten years were found at autopsy to have been due to syphilitic endarteritis of the large arteries at the base of the brain.

Hydrocephalus is associated with, and apparently caused by, congenital syphilis in some cases. Amongst thirty cases of hydrocephalus under my own observation two were certainly syphilitic, one had disseminated choroiditis and therefore was almost certainly syphilitic, and a fourth was sister to a child who had interstitial keratitis. The enlargement of the head in these cases may be present at birth or may begin—as would seem to be more usual—some weeks or months after birth. For instance—Ellen A. had a rash on the buttocks and some desquamation of the palms and soles during the first six weeks of life, and snuffles before she was three months old; at about nine months of age her head was noticed to be growing large. When first seen by me, at fifteen months, the infant had considerable hydrocephalus with some nystagmus and marked choroiditis. Dr. Ashby[44] records a case in which the hydrocephalus began in a syphilitic infant at the age of three months, and mentions a case of Heller's in which the hydrocephalus appeared between the fourth and the seventh months. Sandoz[45] records very fully four cases in which the enlargement of the head was present respectively at nine weeks, at six weeks, a few days after birth, and about fourteen days after birth; the first three of these were examined post mortem, and in all there was thickening of the ependyma of the lateral ventricles, which in two cases had a yellowish colour and in one was roughened as if studded with sago grains ; the choroid plexus in all was thought to be engorged, and in two had an oedematous appearance. He concludes that the cause of the hydrocephalus in these cases was an inflammation of the ependyma and of the choroid plexus produced by syphilis. The relation of syphilis to hydrocephalus in other cases may be less direct. There can be no doubt that syphilis, like any other condition which causes prolonged impairment of the mother's health, impairs also her reproductive power, so that malformation of the foetus may result, or a similar result may be reached by the action of syphilis upon the embryo itself in the earliest stages of pregnancy ; in either case a hydrocephalus may be produced which is the result of malformation not of any inflammatory process in the child, either before or after birth. So it may come about that the child of syphilitic parents may suffer with hydrocephalus due to such a condition, for instance, as narrowing or absence of the 'iter a tertio', which is in no way characteristic of syphilis, and it is noteworthy that, even when such a cause is present, the hydrocephalus is not necessarily noticeable at birth—it may only attract attention several weeks after birth.

Gumma of the Brain and Meninges. Gummatous inflammation of the brain or the meninges is extremely rare in congenital syphilis. Sir T. Barlow[46] has recorded the case of a male infant, aged fifteen months, who had some weakness of facial muscles and nystagmus. At autopsy small conical tumours were found on the fourth, fifth, sixth, seventh, and eighth nerves, at their superficial origin, which, on section, appeared to be gummatous ; they were associated with endarteritis of the vessels at the base of the brain. A case suggestive of a somewhat similar lesion was recorded by Mr. Nettleship[47]: a girl aged fourteen years, with typical Hutchinsonian teeth and interstitial keratitis. Since the age of ten years she had had paralysis of the third, fifth, and sixth nerves. Cnopf[48] mentions an infant, aged six months, who had convulsions and hydrocephalus ; at the autopsy there were gummata in the corpus striatum on each side, as well as some sclerosis of the cortex.

Epilepsy must certainly be included amongst the effects of congenital syphilis upon the nervous system. Mr. Hutchinson mentions three cases in which this sequence was observed, and I would add that in infancy the child with syphilis seems to be very prone to infantile convulsions.

Cardio-vascular Manifestations. The occurrence of endarteritis has already been mentioned incidentally. Several cases have been recorded in which the arteries of the brain were found to be thus affected. In Barlow's case, to which reference has just been made, the basilar and all the vessels of the circle of Willis were extensively diseased ; these were opaque white and almost cartilaginous in consistence ; the lumen was narrowed by great thickening of the intima ; the small arterioles of the pia mater were found to be similarly affected.

Sutherland and Walker's case, in an infant aged sixteen months, showed very similar changes in the large arteries at the base of the brain, and Chiari[49] has described endarteritis in the vessels in this situation in an infant aged fifteen months. Carpenter, in a case of syphilitic nephritis in an infant aged five months, found the arteries in the kidney to be affected by some thickening of their walls, chiefly in the media, but also in the intima.

Heart. Affection of the heart itself by congenital syphilis has been observed but rarely. Carpenter[50] quotes Hektoen as having observed interstitial myocarditis in a syphilitic infant aged six weeks ; and Parkinson[51] recorded the occurrence of an inflammatory nodule, apparently of gummatous nature, in the wall of the heart of a syphilitic infant aged three months.

Congenital heart disease has been attributed by some observers to congenital syphilis, but in my own experience the association has been present so rarely that I cannot but think that it may have been merely a coincidence. It is quite likely that syphilis may, as I have already suggested, like any other condition which interferes with the health of the mother, interfere with her power of perfect reproduction, and so favour the occurrence of congenital anomalies in her offspring. In this indirect manner it may be one of many causes of congenital heart disease, but even so I think the relation is rare; congenital heart disease occurs far more often where there is no family history of syphilis.

Apart from such gross lesions as these, there are other manifestations which are occasionally met with in congenital syphilis connected with the blood and vascular system. Anaemia of a very profound degree occurs during later infancy: the colour is often a yellowish, ivory colour, but much whiter than is intended by the term 'café-au-lait', which refers rather to a brownish, muddy colour, which is seen chiefly with the marasmus of this disease. The mucous membranes are extremely pale; the spleen shows no special enlargement beyond that which is commonly present in congenital syphilis without anaemia. According to R. Hutchison[52] the anaemia in these cases, like any other secondary anaemia, shows no characteristic type of blood. In the milder cases there is diminution chiefly of haemoglobin, with some diminution of red corpuscles; in the more severe there may be also poikilocytosis. In a child, Doris G., aged two and a half years, who was one of twins, and had been preceded by two miscarriages, there were marked Parrot's nodes, and the yellowish colour of anaemia also suggested syphilis; the blood showed haemoglobin 40 per cent., red blood corpuscles 3,032,000 per c.cm., white corpuscles 15,500 per c.cm., colour index was 0·6, differential count of white corpuscles showed polymorphonuclear 61 per cent., large mononuclear 2·5 per cent., small lymphocytes 32 per cent., large lymphocytes 3 per cent., eosinophiles 1·5 per cent.

The anaemia in these cases is not progressive, and although it may last several months, there is, under suitable treatment, complete recovery. Hutchison considers that syphilis acts both by increasing blood destruction and by interfering with its formation.

The relation of congenital syphilis to the so-called splenic anaemia of infancy is still in dispute. My own experience leads me to believe that both syphilis and rickets play some part in its production—certainly either or both may be present—but that splenic anaemia also occurs independently of these diseases. Hutchison states that out of forty-two cases of splenic anaemia in infants congenital syphilis was undoubtedly present in six, doubtful in fifteen, and could be excluded in twenty-one. He considers that syphilis, like any other debilitating condition, may predispose a child to splenic anaemia, but that there is no direct relationship between them.

Haemorrhage in the new-born has been attributed by some to congenital syphilis, and the term 'syphilis haemorrhagica neonatorum' has been invented to denote the association, perhaps with hardly sufficient reason, for it is quite clear that spontaneous haemorrhage in the new-born is not associated with syphilis in the large majority of cases. Abt[53] found that two out of twelve cases were attributable to syphilis; Wilson[54] records ten cases in which syphilis was known to be present in the parents or was evident in the child; these ten occurred among forty-five cases of haemorrhage in the new-born at the Philadelphia Lying-in Charity. Machell,[55] on the other hand, among fourteen cases found none with evidence of syphilis in the child or in the parents. The haemorrhages in these cases have been from the stomach, the bowel, the cord, the umbilicus, and sometimes into internal parts, the meninges or the viscera, and sometimes into the skin. Mraček has found endarteritis of the small vessels in the submucosa of the intestine in some cases of haemorrhage associated with congenital syphilis, but otherwise no explanation has been offered of the association with this disease.

Oedema without albuminuria is occasionally seen in severe cases of congenital syphilis, giving an appearance very like that of acute nephritis. For instance, Beatrice W., aged nine months, was brought for dropsy. She had snuffles, laryngitis, and fissured sores at the anus, and had been wasting. There was oedema, especially of the lower limbs and the lumbar region, with some puffiness of the face; the urine contained no albumen. No doubt the oedema in such cases may not be due to any syphilitic lesion, for it is seen in marasmic infants without any suspicion of syphilis, but its occurrence is noteworthy, for it warns against a hasty diagnosis of nephritis.

Disturbance of Nutrition. One of the most serious effects of congenital syphilis in infancy is the production of marasmus, which is apt to prove very intractable. Any severe disease in infancy may interfere with nutrition and produce more or less wasting, and in this way the infant who suffers with severe manifestations of syphilis is likely to waste, but the marasmus is an indirect result. It is not essentially syphilitic in causation, and is certainly not of the sinister significance which belongs to the true syphilitic marasmus. The marasmus which is directly due to syphilis is accompanied sometimes by little or no other evidence of the disease, although the history of previous miscarriages or still-births may make it almost certain that syphilis is present; characteristic manifestations of the inherited taint may only appear after the marasmus has already been present some time. It begins usually, I think, within the few weeks following birth, and is often said to have begun from birth; the infant is 'a fine baby born', but it begins to waste directly after birth in spite of breast-feeding with milk which appears to be of good quality.

The wasting continues until the infant is reduced to a shrivelled, monkey-like little creature, by which time there may be a hoarse cry and snuffles, and perhaps a rash. If the cause of the marasmus has been recognized, mercury has been given, and although this may cause subsidence of the other syphilitic manifestations, the wasting is apt to continue until, in spite of all treatment, the infant dies of exhaustion.

There is another curious interference with development which may result from this disease: the child's growth is stunted and the phenomena of puberty are delayed several years beyond the normal time. In this way a boy of seventeen or eighteen years may look as if he were only eleven or twelve years old. This condition has been described as syphilitic infantilism. In the cases of juvenile general paralysis to which I have referred above, it is usual for the puberty changes to be much delayed.

No lesion of the gastro-intestinal tract has been demonstrated to account for the marasmus of this disease, and indeed it is remarkable how little the stomach and bowel are affected by congenital syphilis. I have referred to Mraček's observation on the syphilitic endarteritis in the submucosa of the intestine which is found in some cases of melaena neonatorum. Apart from this observation I know of no evidence that any organic syphilitic lesion occurs in the stomach or intestine in the inherited disease.

The peritoneum seems to be rarely if ever affected. Henoch described one case in which the abdomen became enlarged and extremely tender at the age of four weeks in an infant with well-marked evidence of syphilis; the peritonitis, if such it were, gradually subsided, and the infant recovered. I have recorded [56] the case of a male infant who showed evidence of syphilis during life, and died at the age of four weeks with acute peritonitis. At the autopsy, in addition to acute peritonitis, intercellular cirrhosis of the liver was found. It might be expected that peritonitis would sometimes be due to congenital syphilis in infancy and childhood, if it be true that syphilis may cause peritonitis in intra-uterine life, as some observers have held. In examining the body of a still-born infant whose birth had been hindered by foetal ascites, I found the intestines matted together by adhesions. The liver showed intercellular cirrhosis.

Affections of Bones and Joints. Amongst the commoner manifestations of congenital syphilis must be reckoned the affections of the bones and joints: the commonest are epiphysitis and chronic periostitis.

Epiphysitis occurs most often within the first three months of life. It was present in eleven per cent. of my cases. Scherer found it eleven times in fifty cases of congenital syphilis, i.e. in twenty-two per cent. Bednar, according to Coutts, found it in nineteen out of sixty-eight cases. In my own cases the arms were affected either alone or with the legs in eight out of eleven cases. The legs were affected in three cases alone, in three others with the arms.

In Bednar's nineteen cases, the arms were affected sixteen times, the legs once, and all the limbs twice.

The first indicationof its presence is loss of power, or at any rate failure to move the limb. At first there is little or no swelling to be detected about the epiphysis, and the condition simulates a true paralysis and has been described by Parrot as 'syphilitic pseudo-paralysis'. In some cases, however, which are not treated early, considerable thickening can be felt and may even be visible at the epiphysial line. I think there can be no doubt that occasionally, perhaps very rarely, suppuration occurs at the epiphysis in these cases, but it may be that this is due rather to a secondary infection of the inflamed epiphysis by pyogenic micro-organisms than to syphilitic inflammation. The following is a typical example of syphilitic pseudo-paralysis: Herbert S., aged two months, began to scream fourteen days ago when his arms were moved, and seemed to have lost the use of both arms. He has had snuffling from birth but has had no rash; some thickening is felt about the upper epiphysis of the left humerus and also about the upper epiphysis of the radius in each forearm; there is no movement of the arms or forearms; the child cries if they are handled. The mother was treated ten months for syphilis about three years ago; she then gave birth to a child who had snuffles severely and died at five weeks; the patient was the next child. Inunction of mercury over the abdomen produced rapid diminution of the epiphysial thickening and also of tenderness, and seen about a week after the treatment was begun there was already slight movement of fingers and wrists, and a week later there was good movement of the upper limbs. In some cases no thickening whatever can be detected, the loss of movement is the only symptom. It is obvious that such a condition might be mistaken for infantile paralysis, or when there was definite thickening, it might closely simulate infantile scurvy. From both these diseases it is distinguished usually by the earlier age at which it occurs; infantile paralysis and scurvy are both extremely rare under the age of five months; it may be doubted, indeed, whether scurvy ever occurs under five months: the localised tenderness and thickening, if present, serve to distinguish it from infantile paralysis, whilst the localisation of the thickening strictly to the epiphysial line distinguishes it from the more diffuse thickening of scurvy which extends usually along the shaft of the bone. If it were possible to test the tendon jerks and the electrical reactions, the absence of the former and the characteristic changes in the latter would point to infantile paralysis, but it is neither necessary nor practicable usually to test these points, the pain and tenderness forbid any unnecessary handling, and there is almost always ample evidence of syphilis in the child or in its family history to make the nature of the affection sufficiently obvious.

It has been pointed out by Coutts that pseudo-paralysis is present sometimes with no palpable thickening at the epiphysial line and no tenderness, and he suggests, therefore, that as the loss of movement cannot be due to pain it may be due to an affection of the peripheral nerves in association with some epiphysial inflammation. Bednar, he says, ascribed it to a syphilitic myositis. Certainly it is remarkable how in some cases there is nothing to be detected beyond the loss of movement; the condition is often diagnosed as 'epiphysitis' rather because the combination of rapid loss of movement in one or more limbs with congenital syphilis has been attributed to this lesion than because there is any proof of epiphysial inflammation. This only is clear, that the lesion, whatever it may be, is capable of very rapid recovery under the influence of mercury, and that there is very little tendency to relapse. I have never seen any occurrence of relapse myself. Dr. A. M. Gossage [57] has recorded a case in which a boy aged seven weeks lost the use of the arms and legs from syphilitic epiphysitis; under treatment he improved rapidly but the mother ceased to bring the child for treatment after nine weeks, so that no mercury was given for three months: at the end of this time the right leg again lost power with fresh epiphysitis.

Continental observers have described a more insidious affection of the epiphysis, which is said to be almost invariably present in syphilitic infants who are still-born or die shortly after birth: there is slight swelling at the junction of epiphysis and diaphysis, and on section 'a narrow somewhat jagged line of yellowish or orange-colour' is seen running along the margin of the epiphysial cartilage (Henoch). This appearance is stated to be due to proliferation of cartilage cells, arrest of formation of new blood-vessels and consequent degeneration of the proliferated cells. It is even stated that as a result of these degenerative changes separation of the epiphysis may occur; but it is admitted that in the majority of cases no symptoms whatever are produced by this affection. Such is the lesion which Wegner[58] first described and which some writers have considered so essential to the post-mortem recognition of congenital syphilis that its absence is almost conclusive evidence of the absence of syphilis. I can neither affirm nor deny the existence of such appearances as this, but I can state positively that they are by no means always present in syphilitic infants and I doubt whether they are even usually present. I have sought them repeatedly without finding them in cases of undoubted syphilis.

It seems likely enough that congenital syphilis may affect the development of bone in utero, either directly by causing some inflammatory process in the growing tissue or indirectly by impairing the mother's power of reproduction, so that some perversion of bone formation occurs exactly similar to that which is seen in some cases where parental syphilis is absent, but where the mother's health is impaired from other causes. Such an affection is shown in the accompanying skiagram (Plate LX) of a case recorded by Dr. G. A. Sutherland[59] in which there seemed to be evidence of parental syphilis. The bones of the limbs show multiple fractures which are not situated at the epiphysial junctions, the bones are also much bent, and show abnormal thickenings, some of which do not appear to be due to callus but rather to abnormal formation of the bones. A very similar case was reported by Dr. L. Guthrie[60] of fragilitas ossium syphilitica with multiple fractures, probably congenital, in a male infant aged two months who had a syphilitic ulceration on the buttocks and make a speedy recovery on mercury.

Dactylitis must be classed among the early manifestations of congenital syphilis. It was present only in two out of 100 cases under my own care. Of nine cases which I was able to collect, including the two cases mentioned and seven published records, none were over two years of age, seven were under one year old, the earliest were two which occurred at the age of four weeks. In most cases the fingers were affected; much less often the toes; in one case (Carpenter) the metacarpal bones. As a rule more than one finger is affected but usually only one phalanx in a finger, and that the proximal one. The disease may affect both hands but there is no special tendency to symmetry so far as I can ascertain, although some writers have laid stress upon this as a distinguishing point between the dactylitis of syphilis and that of tubercle. If no anti-syphilitic treatment is used the swelling of the finger increases, the superficial parts become discoloured with reddish-brown colour, and a discharge of broken-down tissue occurs as happens with gummatous conditions in other parts of the body. The swelling appears as a more or less fusiform thickening of the phalanx, which in some cases appears to be most marked near one or other end of the bone, as if the inflammatory process had started in connexion with the epiphysis, but there is considerable difference of opinion as to the nature of the lesion; some writers assert that it is an epiphysitis, others that it is a periostitis, and others that it is primarily an osteomyelitis. Actual observations of the morbid anatomy of this condition are wanting. Periostitis of a chronic kind is not very rare in congenital syphilis. It occurs usually later than the epiphysitis and dactylitis which have just been described. In some cases it appears clinically as a diffuse thickening along the shaft of a bone, perhaps most commonly the tibia; in others it is a more localised process, a rounded boss-like tumour appears, which may undergo a process of softening and discharge superficially or may cause absorption of the bone over which it occurs: in either case the process is no doubt a gummatous periostitis.

In the tibia chronic periostitis affects chiefly the middle third of the diaphysis and is recognized clinically by the convexity which it gives to the anterior edge of the tibia, thus producing the appearance described as ‘sabre tibia’; there is sometimes complaint of vague aching pain in the legs, and some slight tenderness when it is handled; but there is no acute pain or tenderness. Usually both legs are affected, but not always. A similar condition occurs in the other long bones. In most cases this thickening reaches a stage in which it remains stationary without showing any tendency to soften, but occasionally the superficial structures have become inflamed and there has been discharge of softened puriform material, and under these circumstances the surface of the bone may be felt at the bottom of the sinus to be bare and evidently necrosed.

With periostitis there is associated in some cases an inflammation of the bone also, which may produce a softness, so that the bone bends easily, and may, perhaps, as a subsequent change, give rise to sclerosis of the bone, so that it becomes abnormally dense and hard.

A syphilitic osteitis affects the flat bones in some cases. A boy aged ten months was under my care with a syphilitic rash, laryngitis, and condylomata at the anus. He had also choroidoretinitis ; just in front of the frontal eminence on each side there was a triangular gap in the bone ; this triangle measured about an inch vertically from the apex, which was above, to the base below, and about one inch along its base, which was about half way between the scalp and the eyebrows. The bone appeared to be entirely absent in these areas, and I supposed it was a congenital anomaly of ossification ; but the child was treated with mercury and iodide for the other syphilitic manifestations, and within a few weeks the gaps had been completely filled up with hard bone with a slightly uneven surface. In this case no swelling had been noticed over these areas, so that it would seem that the bone may have been absorbed by inflammation in its substance rather than by a gummatous deposit outside. It was impossible, however, to exclude the possibility of gummatous periostitis on the inner side of the skull, and Henoch mentions that Wegner observed such deposit both on the inside and on the outside of the skull. Barlow[61] has recorded the case of an infant, aged six and a half months, who, with other evidence of syphilis, showed at least five round areas of localised periostitis on the outside of the skull, and at one of these the bone had been destroyed, so that for an area covered by half a crown the dura mater was exposed, and presented a granular surface. I have seen one case in which an infant, aged seven months, with snuffles and enlargement of the spleen, whose mother admitted having had syphilis, showed a rounded swelling connected with the sternum, which I took to be a gumma. Henoch has recorded an instance of superficial necrosis of the sternum, apparently produced by gummatous periostitis, in an infant aged eight weeks, who showed definite evidence of syphilis later, but no proof of it at the time, so that Henoch considers the nature of the case as uncertain.

I turn now to a vexed question, the nature of craniotabes and bossing of the skull, the so-called 'Parrot's nodes'. It has been affirmed by some observers, and has passed into tradition, that craniotabes is the result of syphilis (see Plate LXI).

Probably no investigations have done more to support the view that craniotabes is the result of syphilis than those of Barlow and Lees,[62] who found evidence of syphilis in 47 per cent. of cases of craniotabes and concluded that 'syphilis is by far the largest factor in the causation of craniotabes'. Carpenter found that 74 per cent. of cases of craniotabes showed evidence of syphilis. On the other hand, Elsässer, who first described craniotabes in 1843, regarded it as rachitic. My own observations lead me to regard craniotabes as much more often a manifestation of rickets than of syphilis; indeed, on examining the skull clinically in large numbers of infants, I have been struck with the unusually firm ossification of the skull in many syphilitic infants at a very early age. The difference of opinion arises, I think, from a difference of view as to what constitutes craniotabes. If diffuse yielding of the skull on pressure, especially near the edges of the parietal, be taken to indicate craniotabes, then the term may mean nothing more than the delay of ossification which is to be found sometimes in infants who show no disease at all; but if the term be strictly limited to cases in which there are islands of parchment-like bone, surrounded by firm, well-ossified bone, the condition which post mortem shows absorption of the skull from within, a real tabes of the cranium, a loss of already-formed bone, then I think it will be found that craniotabes most often occurs with rickets alone, and that when it occurs with syphilis there is also rickets associated with the syphilis.

There can, I think, be no doubt that the combination in which craniotabes may be looked for with the strongest probability of finding it, is with laryngismus stridulus, which is admittedly one of the nervous disturbances of rickets, and has no connexion with syphilis. Moreover the craniotabes in these cases disappears very rapidly under anti-rachitic treatment. As Carpenter points out, craniotabes was found by Mr. Bland Sutton in rickety monkeys where freedom from syphilis could be guaranteed. Where syphilis is combined with rickets, the symptoms of rickets are aggravated, and in this way syphilis may contribute indirectly to the causation of craniotabes : and it is to be remembered that this combination is not uncommon. Monti, indeed, stated that he had never seen syphilis without rickets, a statement which I cannot endorse, although I am satisfied that the combination occurs fairly often. Syphilis, however, is far less frequent than rickets, so that rickets is usually found without syphilis; but craniotabes is often present, nevertheless, in these cases of pure rickets.

Bossing of the skull was described by Parrot as evidence of congenital syphilis. The typical condition is the occurrence of four rounded boss-like elevations on the vertex of the skull, adjoining the anterior fontanelle ; so that an appearance like that of a hot-cross bun is produced, the anterior fontanelle being at the intersection of the cross ; in some cases only the two anterior or the two posterior bosses are present. Again, the question arises whether such a condition is always evidence of syphilis, or whether it may be due to rickets. Coutts lays stress upon the position of the bosses. He says that the natiform skull, with the four bosses surrounding the anterior fontanelle, is undoubtedly syphilitic, whereas the cranial bosses in rickets are confined to accentuation of the frontal and parietal eminence, parts not affected by the syphilitic thickening ; but where rickets is combined with syphilis a mixed type of skull results, in which it is difficult to determine the part played by each factor. The cranial bosses in syphilis, he says, do not often last beyond the first year of life, and leave no traces of their former presence. My own observations lead me to doubt whether any such pathognomonic significance is to be attached to the 'natiform' or 'hot-cross-bun' skull; clinically, at any rate, cases occur in which such a condition is found with severe rickets but with no evidence whatever of syphilis. It is possible that there may be a difference between the rachitic and the syphilitic thickening anatomically; at any rate, it is quite certain that in some cases the thickening is found to be due to an increase chiefly in the diploe of the skull, which is extremely red and vascular, while the outer surface of the thickened part remains smooth and normal in appearance, except for the purple colour showing through, which indeed may be visible through the scalp during life. In other cases the thickening is due to deposit of new bone on the outside of the cranium, which has a rough, honeycomb appearance, due to a very vascular growth of new spongy bone ; this latter condition is certainly found in syphilitic infants. I am not aware that it is ever found in pure rickets.

The question must remain *sub judice*, but I think that it may at any rate be fairly said that there is not sufficient evidence to justify a diagnosis of syphilis from the presence of Parrot's nodes, even when they are present in most pronounced degree and adjoining the anterior fontanelle.

Joint Affections are not so rare as has been supposed in congenital syphilis. Amongst one hundred consecutive cases I saw seven with chronic affections of joints, and one with suppuration in joints secondary to syphilitic epiphysitis. In three of these cases, a girl aged seven and a half, a boy aged nine, and a boy aged seven and a half, the affection was a chronic synovitis with effusion in both knees, in the third case also in the ankles ; all three had interstitial keratitis. The four remaining cases resembled rather an osteo-arthritis than a simple synovitis. All were boys, aged respectively five and a half, six, nine years and eleven months, and six years. All had syphilitic eye lesions, three showing interstitial keratitis, and the fourth an old iritis with some keratitis which was thought to be superficial, although he suffered with gummata on the bones and in the viscera and was severely syphilitic. In this syphilitic osteo-arthritis there is, in addition to chronic effusion with thickening of the capsule in the medium-sized and larger joints, definite bony thickening and lipping, which affects also the smaller joints. This osteophytic change may even simulate Heberden's nodes, as I saw in the fourth case mentioned here, where some of the distal phalanges showed lateral thickenings very like Heberden's nodes. They were, however, less regular in their distribution, for they occurred not only on the distal, but also on one or two of the proximal phalangeal joints, and the toes showed similar nodosities. The deformity about the joints causes slight limitation of movement and is persistent for some years, but in cases under my observation has seemed to diminish rather than to increase after the lapse of a year or two. There was no enlargement of the glands. I have recorded such a case more fully in 'The King's College Hospital Reports', vol. vii, p. 366. Fradley and Riddell[63] record the case of a girl, aged nine, whose knees became affected at the age of seven, and subsequently, within a few months, all the joints of the limbs, including some of the finger-joints. There seemed to be bony thickening about some of the joints, but this could not be detected in skiagrams. The authors describe the case as 'gummatous synovitis simulating rheumatoid arthritis.'

I know of no post-mortem observations on these cases, unless the cases described by Mr. Bowlby[64] be of this nature; but there can, I think, be no doubt that there are changes in the cartilage, and probably in the bone, in these cases.

Although amongst my small number of cases of joint affection there were more cases of this syphilitic osteo-arthritis than of simple synovitis, the latter is probably the less rare. Dunlop[65] quotes Von Hippel as finding joint affections in 56 per cent. of cases of congenital syphilis. Dunlop was able to collect sixteen cases from his own practice and that of his hospital colleagues at the Sick Children's Hospital, Edinburgh. He mentions as the chief characteristics of this syphilitic synovitis, its insidious development, its chronic course, its symmetrical distribution, its freedom from pain, and the mobility of the joints on passive movement, its association with other syphilitic stigmata, its amenability to treatment, and its tendency to relapse. He says that it occurs usually between the eighth and the thirteenth years, but may begin as early as three and a half years and as late as the eighteenth year. The knees are affected much more often than any other joint, and in forty-three cases recorded by Von Hippel the knees were affected forty-one times, and in thirty-five the knee was the only joint attacked. Mr. Clutton[66] also observed a symmetrical synovitis of the knees several times in congenital syphilis. Dunlop states that in some cases the only change found has been slight hyperaemia of the synovial membranes, but that in others this membrane has been infiltrated with gummatous material, and synovial fringes, swollen and gelatinous, reddish and sometimes greyish-white, resembling broken-down tubercle in the centre, hang down into the joint cavity.

The difficulty of diagnosis between such an affection and tubercular disease of the joint would be very great if the synovitis were the only lesion present; probably the symmetry of the distribution, and perhaps the absence of pain, and the absence of any tendency to destructive change or suppuration, would point to syphilis; but fortunately the nature of the joint affection is almost always clear on account of its association with other more characteristic manifestations of syphilis, particularly with the eye changes of syphilis.

CHAPTER XXIV

PATHOLOGY

The pathogeny of inherited syphilis is no doubt identical with that of the acquired disease, and if the causal relation of the *Spirochaete pallida* to the acquired disease be confirmed, then it may be concluded that the same organism is responsible also for the inherited disease. That this spirochaete is present in the bodies of children dying with congenital syphilis has been abundantly demonstrated (see Plates XIV–XVI). The whole subject of the spirochaete and its relation to syphilis has already been considered fully by Professor Metchnikoff, but here I may mention some of the observations which have been made upon its occurrence in congenital syphilis. In the first place the most natural mode of transmission from the mother would be by the blood; and one would expect, therefore, that the specific organisms would be found in the placenta and in the umbilical cord. Simmonds [67] found the *Spirochaete pallida* in the latter situation in two cases, and in the placenta in one of these; the same observer found the organism in four macerated syphilitic foetuses.

Thomsen and Chievitz [68] found the *Spirochaete pallida* only in one out of five macerated syphilitic foetuses, but in nine out of ten unmacerated foetuses.

In the syphilitic infant after birth, Ravant and Ponselle [69] found the spirochaete in the blood shortly before death. Most of the cases reported hitherto have been fatal cases, and the spirochaete was found in the viscera after death. Levaditi and Sauvage found this organism in the heart blood, in the bullae of pemphigus, and even in the normal skin of infants dead of congenital syphilis, whilst the former observer with Salmon states that they are also found in the lungs, liver, and suprarenal capsules. Reischauer found them in film preparations from the spleen, lung, and liver, and especially in the last-named organ, in a still-born infant whose mother had syphilis. Levaditi has shown that the spirochaete is to be found chiefly in those organs which are known to be most often affected by syphilis, and considers that this excludes the possibility that the organism may indicate only a secondary infection. Moreover, he says that the frequency of the spirochaete in still-born infants and in those who have died after the first few inspirations, and have received nothing into the alimentary tract, is opposed to this view. The *Spirochaete pallida* is carried by the blood stream, but quickly makes its way out of the blood-vessels and attacks especially glandular epithelium, penetrating the protoplasm of epithelial cells, such as those in the liver and suprarenal. Menetrier and Duval were able to diagnose syphilis in an infant who died twelve hours after birth with no symptoms beyond three or four bullae on the sole of each foot. Numerous groups of *Spirochaete pallida* were found in the bullae, and in the suprarenal capsules. Beitzke failed to find the spirochaete in spite of most careful search in four cases out of eighteen examined ; but these exceptions he considers are not sufficient to discredit the causal relation of the organism to congenital syphilis. He examined also four new-born infants, who had died of causes other than syphilis, and failed to find a single spirochaete in any of them. In three infants who had suffered with congenital syphilis, but had been so thoroughly treated that all symptoms had disappeared before they died of some other disease, careful examination of the viscera failed to detect the spirochaete.

The finding of the *Spirochaete pallida* by so many observers in the tissues of infants with congenital syphilis, when considered in connexion with the finding of the same organism in cases of acquired syphilis, is at least suggestive of a causal relation; but the time is certainly not ripe for any dogmatic statement on this point.

We are on firmer ground when we come to consider the morbid anatomy of inherited syphilis : and we shall do well to consider first syphilis as it affects development. The placenta is said by Ballantyne [70] (from whose admirable account I shall take most of the facts connected with the foetus and placenta) to be larger and softer than normal, and shows pale yellowish patches in its substance ; its vessels show endarteritis and consequent narrowing of the lumen, especially in the villi, which are enlarged and fibrosed. In the maternal portion of the placenta there are sometimes haemorrhages which also interfere with the circulation through the placenta, and so favour the death of the foetus. In the cord also there is endarteritis, and thrombosis may occur, so that the foetus is deprived of a proper blood supply and is likely to die. Hydramnios is associated often with foetal syphilis. Ballantyne suggests that this may be due to increased pressure in the umbilical vein caused by lesions in the placenta, in the cord itself, or in the foetal liver, and may be comparable to portal ascites.

With regard to the foetus itself it may be pointed out first that a macerated foetus is not necessarily a syphilitic foetus, nor is a syphilitic foetus necessarily a macerated foetus. It is also to be remembered that the still-born foetus of a syphilitic mother may show nothing abnormal in many of its organs, or in any at all. In the lung, according to Ballantyne, four different lesions are found : (1) a generalized diffuse gelatinous infiltration, pneumonia gelatinosa ; (2) the so-called pneumonia alba, in which there are thickened patches, white in colour, and consisting of air vesicles crowded with epithelial cells in a state of fatty degeneration ; (3) scattered miliary gummata with signs of interstitial pneumonia about them ; (4) a definite interstitial fibrous pneumonia, due to hyperplasia of the pulmonary connective tissue. The liver may show only microscopic changes, increase of fibrous tissue in the portal areas and some ‘ generalized infiltration with embryonic cells ’ ; or there may be groups of cells, which, if sufficiently numerous, give rise to the ‘ semolina grains ’ which are sometimes visible with the naked eye on the surface and in the substance of the liver. The spleen is almost always enlarged in the syphilitic foetus. The kidneys are said to show endarteritis and periarteritis, and often some proliferation of interstitial connective tissue. Peritoneal adhesions are sometimes found. The bones are said to show the osteo-chondritis which was described by Wegner, visible as a yellow line across the bone where the osseous joins the cartilaginous tissue.

This, in brief, is the morbid anatomy of the syphilitic foetus. I turn now to that of the syphilitic child who has lived long enough to develop the post-natal manifestations of the disease. Probably the most characteristic lesion is the cirrhosis of the liver, which differs from that due to other causes in its uniform diffusion, so that the fibrous proliferation passes even between the individual cells of the organ, constituting a truly intercellular fibrosis. The liver is enlarged, generally smooth on the surface, not actually hard, but tougher than normal. On section it is sometimes not possible to detect the cirrhosis with the naked eye, although it may be quite obvious with the microscope; sometimes the liver has a rather greyish appearance on section, and some of the larger strands of fibrous tissue may be detected by the naked eye. On microscopic examination the fibrous tissue in the portal areas is seen to be increased, and continuous therewith a stroma of loose fibrous tissue passes between the cells dividing them up, so that groups of two or three may be left contiguous in some parts, while in others single cells seem to be surrounded by the meshwork of fibrous stroma.

The cells, moreover, are of very irregular shapes, and many of them have a blurred appearance, have lost their nuclei, and stain badly, as if degenerated. Owing to the separation of the cells, the lobular arrangement of the liver is completely lost in an advanced cirrhosis, and in any case may be lost in parts while it is retained elsewhere, for it is very striking in some cases that the cirrhosis is more evident in some parts of the liver than in others; it is often specially well marked near the portal areas.

With or without such a cirrhosis there are found gummata in the liver which have the character of gummata elsewhere; to the naked eye the gummata in the liver have a pale yellowish, or orange-yellow, or buff colour, and although circumscribed and usually more or less rounded in shape, are not enclosed by any real capsule; they consist of a collection of small round cells, with a stroma sometimes of fine fibrils, and in the centre the cells are degenerated, or only nuclei may be visible with some débris and fat globules. At the outer part of the gumma, which passes almost imperceptibly into the tissue of the liver, there are dilated vessels and apparently new blood-vessels visible among the cells of the gumma; the cells are for the most part small round cells like those met with in any inflammatory process, but there are also other larger and occasionally some irregularly-shaped large cells, like the so-called 'giant cells' of tubercle.

Dr. Rolleston has recorded a case in which the common bile duct was obstructed by inflammation of its wall in a syphilitic infant aged three weeks. I am indebted to Dr. Rolleston for permission to show here drawings (see Plate LXII, Figs. 1, 2) of the affected bile duct, in the wall of which is seen a mass of granulation tissue obstucting the lumen. The infant had become jaundiced seven days after birth, and continued so until its death at the age of three weeks.

In the liver, as in other organs, there has occasionally been found lardaceous[71] degeneration, but it is extremely rare in congenital syphilis. I have recorded such an occurrence in a boy aged eleven years, and Dr. Ashby[72] has recorded it in a girl aged ten years, whose liver was not only lardaceous, but showed fifteen or sixteen gummata. Coupland[73] mentions two cases recorded by Laschkewitch, the one a girl aged twenty-two years, the other a boy aged fourteen years, both with congenital syphilis.

The spleen is usually found to be enlarged, but not very greatly. The nature of the enlargement is described somewhat differently by different observers. Some have attributed it to a simple hypertrophy, a hyperplasia of all its component parts, others to a condition comparable to the cirrhosis of the liver; the fibrous trabeculae according to these observers, are thickened and the fibrous stroma of the spleen increased; the capsule is thickened. Gummata, as already mentioned, are very rare in the spleen in congenital syphilis. In 1897 I could only find four cases recorded, in addition to two which I reported to the Pathological Society.

The suprarenal was found to have undergone a cirrhotic change in an infant aged five weeks with inherited syphilis:

Dr. Carpenter,[74] who records the case, states that the suprarenals were adherent to the kidneys, enlarged and of opaque yellowish-white colour; on microscopic examination chronic inflammatory changes were found. The suprarenal cirrhosis was associated in this case with interstitial nephritis.

The kidney may be the seat of a diffuse inflammation or may show localised gummata. Nephritis in congenital syphilis is probably in most cases interstitial or chiefly interstitial, although cases do occur in which the change is purely parenchymatous. Sutherland and Walker describe the changes in their cases as follows: 'The interstitial tissue of the cortex was densely infiltrated with round cells. Here and there the infiltration was so dense that the tubules and glomeruli were obscured. In other areas for the most part subcapsular the infiltration was absent. Fine capillary vessels were found in the infiltrated areas here and there, their contents had escaped into the surrounding tissues. The adventitia of the larger vessels was infiltrated by closely packed small round cells and the media and intima were unchanged. The kidney tubules were widely separated by the infiltrated interstitial tissue. The lining epithelium was somewhat granular in appearance and in many tubules the lumen was filled with casts of homogeneous material or masses of round cells. In the patches of dense infiltration the epithelium was shed and blocked the lumen of the tubule. A few of the glomeruli showed a slight increase in their nuclei but the majority displayed no change. In the medulla, round-cell infiltration was present but only to a slight degree. In this part of the kidney there was engorgement of the blood-vessels and the straight tubules contained casts of round cells.' Two cases which were under my own observation showed very similar change, there was definite tubal catarrh associated with much more striking acute interstitial inflammation, as in the case described by Carpenter[75]: but in one case, which died at the age of two months under my care, the nephritis was purely tubal. Carpenter has also described a case of syphilitic nephritis in an infant aged five weeks in which he considered that the nephritis was tubal only, with no interstitial change. In this case, and

I thought in my own similar case, the arteries showed some thickening of their walls, but apparently rather in the outer coats than in the inner. In two cases recorded by Coupland[76] the nephritis was of the parenchymatous variety: these were girls of thirteen and eighteen years respectively, and both showed gummata in other parts of the body and characteristic clinical evidence of inherited syphilis. When gummata have occurred in the kidney they have been of the small miliary variety. Beer[77] described such a condition in an infant aged six weeks.

The pancreas has been affected with an interstitial fibrosis, but this is probably extremely rare. Rolleston[78] has recorded this lesion in a female infant aged three weeks in whom there was also obstruction of the common bile duct by syphilitic granulation tissue. The pancreas in this case was enlarged, firm, and white; and on section of the head of the pancreas there was some interstitial fat necrosis: there was no dilatation of Wirsung's duct. The microscopic changes which are shown in the accompanying illustrations are thus described by Dr. Rolleston.

'The tubules of the gland are invaded and broken up and the acini destroyed or widely separated by connective tissue in various stages of development, round mononuclear cells resembling lymphocytes, plasma cells, spindle cells, and fibrous tissue. Some of the arteries show periarteritis but not endarteritis. The interstitial pancreatitis is so advanced that the normal appearance of the gland is quite obscured' (see Plate LXIII).

Birsch-Hirschfeld found some affection of the pancreas in several infants who were still-born or died shortly after birth, with changes in the bones considered characteristic of congenital syphilis (presumably Wegner's osteochondritis).

The lungs seem to be affected very rarely after birth by the inherited taint; the changes that have been described above as occurring in the foetal lung are mostly not consistent with live birth, or at any rate with prolongation of life beyond a few days; but there are two changes which may begin after birth and may be consistent with life, namely, gummatous deposit and a chronic fibroid pneumonia. Dr. Greenfield, in reporting his case of chronic pneumonia in a child suspected of inherited syphilis at the age of one year, pointed out that the condition is something quite *sui generis*, the walls of the alveoli are remarkably thickened, as are also those of the vessels and bronchi: the thickening of the walls of the alveoli is due chiefly to cell proliferation which almost obliterates many of the alveoli, although the epithelium lining these remains intact. Some fibrous tissue also contributes to the thickening of the alveolar walls as well as to the great increase in the septa of the lung and about the bronchi. It is particularly noteworthy that in Greenfield's case, as in some others that have been recorded, the syphilitic pneumonia was limited to one lung. I know of no post-mortem observations on syphilitic pneumonia in later childhood, but as I have already suggested it seems quite possible that some of the unilateral fibroid affections of the lung in later childhood may be a later stage of this syphilitic pneumonia of infancy; and one may conjecture that it would be characterized by more development of fibrous tissue, less cell proliferation and considerable dilatation of bronchial tubes.

The testicle has shown, in the few cases which have been examined, fibrous thickening of the tunica albuginea, especially at the corpus Highmorianum, and considerable increase of fibrous trabeculae passing through the organ. Carpenter describes and figures sections of such a testicle, showing a large quantity of fibro-nuclear tissue between the seminal tubules. Hutchinson has reported a case of gumma occupying nearly the whole testis and appearing as an opaque yellow mass with no softening, in a boy, whose age is not stated, but whose permanent incisors had already appeared, and who was the subject of inherited syphilis. Carpenter mentions a syphilitic infant, aged nine weeks, in whom a large broken-down gumma was found in the epididymis. Cornel states that syphilitic orchitis may cause degenerative changes in the cells of the seminal ducts, which themselves may undergo atrophy.

In the circulatory system changes have been found in congenital syphilis, the least rare of which is thickening of the walls of the arteries, generally an endarteritis but sometimes also a thickening of the middle and external coats. Such a condition has been found in the vessels of the kidney in association with interstitial nephritis in congenital syphilis. It has been found also in the large arteries at the base of the brain as well as in the small arterioles of the pia mater. I quote Barlow's[79] description of the change found in his case: 'On making sections of part of one of the middle cerebral arteries the changes which Heubner has described were found most typically shown. Both the adventitia and the muscularis are infiltrated by a cellular growth, and in some cases the muscularis is quite destroyed by it, but obviously the principal changes have taken place in the intima. The membrana fenestrata forms a perfectly definite landmark on the one side and the endothelium forms an equally distinct landmark on the other. Between these two there is a very large accumulation of spindle-shaped nucleated cells, and it is this growth which gives rise to the main thickening of the vessel. The endothelial cells, which are oblong in shape, present in most cases a smooth surface, but at some spots there are minute fungus-like prolongations inwards from them into the lumen of the vessel.' In another case he found cell-proliferation in the inner coat of the artery narrowing for a considerable distance, and ultimately occluding the vessel. In Chiari's case[80] in an infant aged fifteen months the vessels of the brain showed similar changes. Sutherland and Walker (loc. cit.) found in the large vessels at the base of the brain an infiltration of small round cells in the adventitia with dilatation and increased number of the vasa vasorum. There was similar infiltration of the tunica media and the elastic lamina, while in the intima the endothelium was much thickened and in parts had the appearance of granulation tissue. These observers consider that the change commences as an inflammation in the vasa vasorum rather than, as Heubner[81] supposed, primarily in the intima.

Apparently such an endarteritis may by its narrowing of the lumen of the vessel give rise to atrophic changes in the cortex of the brain. Heubner[82] records a case in which a right hemiplegia beginning at the age of eighteen months was found to be due to an extreme degree of endarteritis in the vessels at the base of the brain, with resulting extensive atrophy and disappearance of grey matter over great part of the left hemisphere. Whether atheroma is produced by inherited syphilis has been disputed, but it seems probable that it may be. Mott,[83] contending that acquired syphilis is a cause of atheroma, quotes also Oedmannson and Birsch-Hirschfeld's observations that atheroma occurs in the umbilical vessels and in the arteries of premature foetuses still-born owing to syphilitic infection. Bruhns,[84] by serial sections through the wall of the aorta, found that in six out of nine infants either still-born or dead shortly after birth with congenital syphilis, there were patches of syphilitic inflammation in the wall of the aorta, in the outer layers of the media, and in the adventitia, especially in the neighbourhood of the vasa vasorum.

In the brain congenital syphilis produces, as has been already described, sometimes microcephaly with wasting and sclerosis of convolutions, sometimes hydrocephalus, and very rarely gummata either in the meninges or in the substance of the brain itself. Henoch records the case of a child, age two years, in whom there had been an unusual psychical condition, alternating precocity and stupidity but without any interference with motility. At the post-mortem several nodular tumours were found about the size of a cherry under the pia mater and in different parts of the cerebrum and cerebellum. They were of a grey colour, and transparent at the periphery; the central part was fatty, and partly calcified. These were examined at the Pathological Institute of the 'Charité' and considered to be gummata.

Probably a more frequent effect of inherited syphilis upon the brain is the change which results in 'general paralysis'. Mott[85] has described the pathological anatomy of this condition in sixteen fatal cases. The dura mater was often found unduly adherent to the calvaria, there was usually excess of fluid in the subdural space, the pia arachnoid was opaque and thickened; in some cases there was wasting of convolutions in some parts of the brain, the ventricles were generally unduly distended with fluid, and in some cases one ventricle was more dilated than the other; the ependyma was granular. In six cases in which the two halves of the brain were weighed the left weighed less than the right. The atrophy of the brain affected especially the frontal and central convolutions. Dr. Mott was satisfied that on microscopical examination, the brain showed the same lesion as in the adult form of the disease.

In the bones the most characteristic change due to congenital syphilis is the so-called 'osteochondritis' of Wegner; at the junction of the cartilage with the bone proliferation of cartilage cells takes place excessively, so that the blood-vessels become compressed, and the cell proliferation being starved of its blood supply degenerates and becomes fatty; hence a yellowish or orange-coloured line is seen at the epiphysial junction considerably thicker than the normal whitish line in this situation. There is some difference of opinion as to how the appearance is produced; it is possible, as Taylor suggests, that the cells may be like those of gummatous infiltration elsewhere rather than derived from the cartilage cells. This change, according to Heubner, may be detected in the syphilitic foetus as early as the fifth month or some months after birth; and he, like other German writers, considers it of great importance in the diagnosis of hereditary syphilis. It is most marked, he says, in the lower epiphysis of the humerus and of the radius, the upper of the tibia, and the costochondral junctions. The degenerative process at the epiphysial line may go on to softening, so that the epiphysis is separated from the diaphysis, and in this softened tissue pyogenic micro-organisms easily find a nidus, so that suppuration due to secondary infection may occur.

Craniotabes and Parrot's nodes have been described above (p. 339). The increased vascularity and thickening which give rise to the bossing of the skull or Parrot's nodes are shown in Plate LXI.

Inflammation of the bone and periosteum in congenital syphilis gives rise to thickening of the bone and sometimes irregularity of its surface. Parker describes a humerus in which these changes had occurred: the lower half of the shaft appeared as if encased in new bone, the outer layer of bone was separated from the shaft itself by a narrow cavity containing soft tissue enclosed by delicate trabeculae; the periosteum could easily be stripped off this outer sheath. The medullary cavity of the bone seemed to be occupied by a light, spongy, cancellous tissue containing dark red marrow. A more localised inflammation is seen in the form of gummata which are found upon any of the bones, and differ in no way from the gummata of acquired syphilis. Whether the inflammation be of the diffuse or the localised variety, softening takes place but rarely in the inflammatory products; when this occurs exfoliation of bone may take place through a suppurating sinus.

CHAPTER XXV

DIAGNOSIS: PROGNOSIS: TREATMENT

In connexion with the individual symptoms some consideration has already been given to the diagnosis of congenital syphilis; here I shall only refer to some special points which call for emphasis.

A diagnosis of syphilis in infancy is, I venture to think, made too often on quite insufficient grounds. Snuffling respiration is by no means limited to syphilis: many perfectly healthy babies show this during the first few weeks of life; the nasal passages at that time are very small, and the slightest catarrh produces 'snuffles'; so that this symptom, taken alone, is of very little value.

Rash about the anus and genitals and down the inner side of the thigh is very common in infants free from any suspicion of syphilis; a dry, glazed redness about these parts is often due entirely to irritation of fouled napkins, and I am much inclined to believe that an absolutely identical rash may be produced, in one case by syphilis, in another by local irritation. This may be only another way of saying that the syphilitic child has a particularly irritable skin; but this, I think, is so. How common it is to find a very characteristic syphilitic rash on the face or other parts of the body, with very ordinary eczema behind the ears, or erythema intertrigo in the groins.

Depressed bridge of the nose has been mentioned, even by some of the highest authorities on syphilis, as if it were present at birth: but is this so? This deformity of the nose is attributed by most observers to destructive syphilitic disease of the bones which support the bridge of the nose, and it is produced during the course of severe 'snuffles'. If, therefore, the deformity is present at birth, this must be due to intra-uterine disease of the bones which support the nasal bridge. As I have already pointed out, I believe that snuffles is occasionally present at birth ; but whilst I would not deny the possibility of sufficient destruction of bone or cartilage to cause depressed bridge of the nose at birth, I know of no single observation proving that any such destructive process occurs in utero. Of this I am certain, that when there are other points raising a suspicion of syphilis in very early infancy, the normal flatness of the bridge of the nose in infancy is often mistaken for the syphilitic depression.

Much has been made of the 'syphilitic wig', the thick dark hair of some syphilitic infants, but it is easy to attach far too much importance to this ; many infants who are perfectly healthy have just as thick and dark a 'wig'.

Enlargement of the spleen is of very little value as evidence of syphilis. When present it is usually quite slight; the edge of the spleen may be felt half an inch or one inch below the costal margin ; but it is common enough to feel the spleen at least half an inch below the ribs in children who are brought for ailments of various kinds quite unconnected with syphilis, and in about half the cases of undoubted syphilis the spleen cannot be felt ; so that it is only as confirmatory evidence when other symptoms of syphilis are present that enlargement of the spleen may be of some value in diagnosis.

Marasmus occurring in a breast-fed infant without evident symptoms of indigestion should always arouse a suspicion of congenital syphilis, and it is to be remembered that the syphilitic marasmus may occur before any other symptom of the disease is present. There is, however, nothing, except the uncommonness of marasmus without obvious fault in feeding or digestion, to distinguish this from marasmus due to any other cause.

Amongst the symptoms which are specially characteristic of syphilis in an infant under the age of three months are pseudo-paralysis and a hard enlargement of the testicle. Infantile paralysis is extremely rare at this age, and, moreover, lacks the localised tenderness which may be present about the epiphysis in the syphilitic pseudo-paralysis; and infantile scurvy, which also produces a pseudo-paralysis which may cause difficulty in diagnosis in later infancy, does not occur at this age. Moreover, the tenderness is usually much more acute in scurvy, and there is a history of scorbutic feeding; further, the gum and renal symptoms of scurvy are quite distinctive; so that the diagnosis of syphilis is usually easy by a process of exclusion, when pseudo-paralysis occurs, as it usually does, at this early age. Similarly, the enlargement of the testis, which might be due to tubercle later on—though even then tubercle more often affects the epididymis first—can hardly be due to anything but syphilis, for tubercle is excessively rare under four months of age. Amongst many hundreds of cases of tuberculosis in the first year of life, I have never seen a case of tubercle of the epididymis or testis under four months of age.

The value of ophthalmoscopic examination is to be remembered in the diagnosis of syphilis, both in early infancy and throughout childhood. There may be nothing to draw attention to the fundus oculi, and yet there may be well-marked retinochoroiditis, or opacities in the vitreous, pointing to syphilis. Iritis also, in early infancy, is very rarely due to any cause other than congenital syphilis.

In later childhood, as Mr. Hutchinson has pointed out, there are three symptoms upon which a diagnosis of inherited syphilis can be established almost beyond dispute, the peg-shaped and notched incisors, interstitial keratitis, and rapid onset of deafness without earache or otorrhoea. These three symptoms have been described as the 'Hutchinsonian triad'. Another symptom upon the importance of which Mr. Hutchinson has laid great stress, is rapid destructive ulceration of the palate; this in later childhood or early adult life is almost conclusive proof of syphilis.

In the late hereditary syphilis, also, the changes in the fundus oculi which have been mentioned above are of great value in diagnosis.

Prognosis. Inherited syphilis is responsible for an enormous waste of life, as is shown by the following figures, in which only those still-births, miscarriages, and early deaths are included which immediately preceded or followed, or formed part of a series immediately preceding or following, the birth of the patient in whose family history they occurred: there were 39 still-births, 36 miscarriages, and 25 deaths all attributable to congenital syphilis in the family histories of 87 children who were under treatment for congenital syphilis; moreover, out of the 87 children themselves, 13 died whilst under observation. In other words, out of 187, born or unborn, 113 were sacrificed through the syphilis of their parents. It is impossible to estimate the mortality from congenital syphilis in this country; there are obvious reasons why syphilis should not appear on death certificates as the cause of death in the many cases in which the particular manifestation is itself sufficient to satisfy registration requirements, for instance, the heading ‘ debility, atrophy, inanition ’ may include syphilitic marasmus, and some of the nervous affections of syphilis, such as hydrocephalus and meningo-encephalitis will usually be registered with no reference to syphilis. So that the Registrar-General's statistics, which show for the whole of London an annual mortality of about 275, and for the whole of England and Wales an annual mortality of about 1,300, from syphilis under the age of five years, probably fall far short of the reality, and certainly give no idea of the enormous waste of life which is entailed each year by the large number of miscarriages and still-births due to this disease. But loss of lives is perhaps not the greatest of the evils which may result from inherited syphilis; such a case as that described by Mott, in which a father and mother died, apparently, from syphilitic disease of the brain, whilst two of their children were imbeciles, and two more showed some mental degeneration, may be an extreme instance of what is probably by no means uncommon, namely, mental defect, congenital or acquired, as the direct result of inherited syphilis; and if we were to admit Fournier's view that syphilis in the parents, or even in the grandparents, is responsible for dystrophies of all sorts in their children or grandchildren, if we were to consider, for instance, that harelip, congenital heart disease, and a large variety of congenital deformities were ‘ parasyphilitic ’, then the results of parental syphilis on the posterity would be even more appalling.

In the case of the individual infant the prognosis depends not merely on the fact that syphilis is present, but on the particular manifestations. There can, I think, be no doubt that the presence of symptoms of syphilis at birth, especially of pemphigus, makes the outlook very bad; and I am inclined to agree with Coutts, who says infants born with unmistakable syphilis speedily die. Marasmus, also, which begins usually very soon after birth, if not actually from the time of birth, is always of very grave significance; very few of such cases survive more than a few weeks or months. Coutts remarks, also, that jaundice in infants with congenital syphilis is generally fatal.

But in the majority of cases, where the milder symptoms only are present, and the child begins to snuffle and then has a characteristic rash at a few weeks old, these symptoms subside very rapidly under mercurial treatment, and if a thorough course of treatment be given in infancy there may never be any recurrence of symptoms. Even where treatment has been continued for many months, relapses sometimes occur, particularly the reappearance of condylomata, but with renewed treatment these rapidly disappear and no further symptoms may arise. There is no doubt that some cases of congenital syphilis show such slight signs in infancy that no treatment is sought; these symptoms disappear spontaneously and no other manifestation occurs until late childhood, when interstitial keratitis begins and is perhaps followed by deafness, and by the occurrence of gummata in viscera or on bones.

Of these late symptoms, interstitial keratitis is of good prognosis. In most cases it disappears entirely after several months; but the deafness remains permanent and complete. Gummata at any age are as readily amenable to treatment with iodides as are those which occur in the acquired disease; even in the liver they seem to give rise to no serious result if recognized and treated. Perhaps the most serious of the late manifestations of the disease is the juvenile general paralysis, or, as I should prefer to call it, the meningo-encephalitis of inherited syphilis, which has been described above. This would seem to be invariably fatal in periods varying from a few weeks up to nine years, and according to both Mott [86] and Watson [87] the later this affection appears the more rapid its course; the former writer says ‘ those which begin at twenty or after last a very short time and take on the acute galloping form of the disease ’.

Treatment. The treatment of congenital syphilis, like that of the acquired disease, consists in the administration of mercury or potassium iodide, but there are several modes of administering these drugs, and there are very important practical questions connected therewith, which must be considered here. In the first place it is to be remembered that in congenital syphilis there is a strange intermingling of secondary and tertiary symptoms: no doubt it is true, on the whole, that in infancy the symptoms are of secondary type, in later childhood the symptoms are mostly tertiary, and in accordance with this generalism it may be said that mercury is the drug required in congenital syphilis in infancy, whereas potassium iodide in needed for the manifestations of the disease in late childhood or adult life. But an infant may be born with gummata in the viscera, as post-mortem observations have shown; and as a clinical manifestation, a syphilitic dactylitis, a chronic periostitis, or even a localised gumma in the testis or elsewhere, may occur; and in such conditions the use of potassium iodide as well as mercury is, I think, of great value. Again, in later childhood, condylomata, a secondary manifestation, may occur in association with lesions of tertiary character, and mercury is then to be given in addition to the potassium iodide. Evidently, therefore, it is not possible to lay down any hard and fast rule limiting the use of either drug to any particular period of the disease or time of life.

As to the mode of administering mercury to children, it may be given by the mouth, by inunction, by dry application or baths, or by intramuscular or intravenous injection. It may be laid down, I think, as a sound rule, that the administration of mercury by the mouth is in every way to be preferred in cases where it is possible and effectual; there are, however, cases in which better results may be obtained by other methods, or by the combination of oral with other modes of administration.

The preparation in most frequent use for congenital syphilis in infants in this country is grey powder, and I know of no better for routine use. It is surprising how small a dose will cause rapid disappearance of the early symptoms of syphilis, ½–¾ grain three times a day is generally sufficient; for a child twelve to eighteen months old a grain thrice a day may be required; and if the preparation is used for older children 1½ or 2 grains three times a day may be given. It is wise to combine with the grey powder a small dose of sodium bicarbonate and pulv. cretae aromaticus, for with this combination there is, perhaps, less tendency to gastro-intestinal irritation; a point always to be considered in the administration of mercury, which, in some infants especially, is apt to set up diarrhoea. This tendency to diarrhoea may be overcome by combining Dover's powder (Pulv. Ipecac. Co.) with the grey powder in suitable doses for the age: an infant aged three months may have Pulv. Ipecac. Co. gr. ⅛, at six months gr. ¼, at twelve months gr. ½, three times a day.

Calomel has been used by some physicians for oral administration, but is altogether less satisfactory than grey powder, for it is much more likely to cause looseness of the bowels; it is used in doses of ⅛–⅙ grain thrice a day.

There are infants who will vomit a dry preparation of any sort, and for these it is necessary to provide a fluid form of mercury, if it is to be given by the mouth. Under these circumstances the Liquor Hydrarg. Perchlor. ♏ v–x ter die will be found useful; but again it has the disadvantage that it seems more liable to set up diarrhoea than is grey powder. To some extent this can be counteracted by giving it with minute doses of castor oil and opium; thus Liq. Hydrarg. Perchlor. ♏ x, Tinct. Opii. ♏ ½, Ol. Ricini. ♏ v, Mucilag. Acaciae ♏ xv, Aq. Aneth. ad ʒj ter die for an infant aged six months.

There are cases in which it is in the highest degree important that the child should be brought under the influence of mercury as rapidly as possible; for instance, where there is syphilitic iritis, or in the case of syphilitic epiphysitis. In these it is best to combine mercurial inunction with the oral administration of mercury. The Unguentum Hydrargyri can be used for this purpose: a piece the size of a large pea (about 20 grains) is to be rubbed gently over the abdomen or over the chest or back at night, and this part is then to be covered with a flannel binder, which is left on until the morning, when the ointment is to be washed off. This inunction may be repeated each night, but the site of application should be varied each night, for the skin of some children is very easily irritated, so that a troublesome dermatitis may be excited. Some prefer to use the oleate of mercury, but if this is used it must be used in smaller quantity.

Another method of application is to bathe the child in a mercurial bath: 20 grains of perchloride of mercury in two gallons of water may be used first, and then increased gradually to 40 or 50 grains to the two gallons. This method has, in private practice, the great disadvantage that it entails the risk of entrusting large doses of such a powerful drug to unskilled and perhaps careless persons; moreover, it is even more uncertain than inunction as to the amount of the drug which may be absorbed.

For several years it has been the practice of some physicians to inject mercury into the tissues in severe cases where rapid mercurialisation was necessary. Henoch mentions subcutaneous injection of perchloride of mercury in doses of gr. $\frac{1}{16}$–$\frac{1}{13}$ for a fortnight; but mentions that once, in a boy aged four years, this treatment produced mercurial stomatitis.

Carpenter quotes Mr. Sidney Stephenson as using a solution of perchloride of mercury, one grain in a drachm of sterilized water. Ten minims of this solution were injected deeply into the gluteal muscle once or twice a week, after carefully disinfecting the overlying skin: twelve such injections, he says, will generally relieve the urgent symptoms of syphilitic iritis.

Intra-muscular injection of biniodide of mercury, $\frac{1}{200}$ to $\frac{1}{30}$ grain in aqueous solution, has also been recommended. A course of ten injections is given at intervals of a few days. One such course may be sufficient, or after an interval of a week or two it may be necessary to give a second course. Succinimide of mercury has also been recommended for intra-muscular injection; it is used in doses of $\frac{1}{6}$ grain dissolved in water.

Intravenous injections of cyanide of mercury, one cubic centimetre of a one per cent. solution may be used : it may be injected at intervals of a few days, and three injections may be sufficient.

It is difficult to find any justification for such painful methods of treatment if other methods free from pain are sufficiently rapid in their action to combat the disease effectually ; and certainly as a routine procedure no such treatment is called for in congenital syphilis at any period of the disease. It is conceivable that in rare instances, for example, in a case of iritis, where there is danger of blockage of the pupil, it might be justifiable to make use of such methods. But such conditions must, assuredly, be very rare ; and it has not been proved that any more rapid effect is obtained by these methods than may be obtained by the combined use of oral administration and the application of mercurial ointment.

For condylomata a very effectual application is a dusting powder of Calomel one part, Zinc. Oxidi. two parts ; or the lotio hydrargyri nigra may be used.

Snuffles is sometimes exceedingly troublesome, owing to the interference with respiration, which makes it difficult for an infant to suck, and prevents it from sleeping soundly. Sutherland recommends for this the dropping of a lotion, consisting of lotio nigra one part, lime-water three parts, into the nostrils. Henoch advises painting the nostrils with a weak solution of silver nitrate if the coryza resists the administration of mercury internally, which is usually sufficient to control the snuffles without local application. A few drops of adrenalin solution (1 in 1,000) dropped into the nostrils may be tried if other remedies fail. The orifices of the nostrils should be smeared with the ointment of the yellow oxide of mercury, if there is any soreness or excoriation.

Epiphysitis in the majority of cases requires no mechanical treatment beyond the protection of the affected limb from injury. It is not necessary usually to apply any splint; the mother need only to be warned that the limb is to be handled very gently and moved as little as possible. The internal administration of mercury, assisted sometimes by potassium iodide, is followed by such rapid improvement that within a week the infant is usually beginning to use the limb again. But there are cases in which a more severe inflammation seems to occur, which may even suppurate. Under such conditions it may be necessary to adopt surgical measures, and splints may be required. For the lesions of tertiary character, such as periostitis or gummata, potassium iodide should be given, with or without mercury ; children stand it well. A dose of 10, 20, or even 30 grains three times a day can be given to a child of five years if necessary. For interstitial keratitis the yellow oxide of mercury ointment should be applied locally, and potassium iodide or a mixture of mercury with iodide should be given internally.

There are some conditions which, though undoubtedly due to syphilis, are not apparently influenced either by mercury or by iodide. The chronic joint lesion which I have described above as simulating osteo-arthritis seems to be uninfluenced by anti-syphilitic treatment. The same is true of most of the cerebral conditions due to inherited syphilis : for instance, juvenile general paralysis, hydrocephalus, and imbecility.

The duration of treatment is a matter of importance. Mr. Hutchinson has expressed himself in favour of continuing the mercurial treatment in infancy only until the symptoms have disappeared. Most physicians have advocated a very much longer course of mercury, some even as long as two years. If treatment is only to continue until symptoms disappear this will mean in many cases not longer than two or three weeks. Such a short course of mercury, in my opinion, is wholly inadequate, and leaves the child liable to a relapse very soon, and probably specially liable to the later manifestations of the disease, which may be so disastrous : for instance, complete deafness or general paralysis. In any case a year's continuous administration of mercury should be given, and my own opinion is in favour of two years if the symptoms have been of any severity. There are cases in which even without treatment the snuffles and rash of early congenital syphilis pass off very quickly, and it may be months or years before other symptoms appear ; but this seems to be no argument in favour of omitting treatment which might prevent these later symptoms from appearing.

Here must be mentioned also the feeding of the syphilitic infant. I have described the marasmus which is a not uncommon result of inherited syphilis in infancy, and have pointed out the very grave prognosis in such cases. The importance of breast-feeding for a syphilitic infant can hardly be over-rated. The chance of recovery is very small if the marasmic infant is deprived of its mother's milk. The mistake is sometimes made of weaning an infant because it has congenital syphilis ; but this should be the very reason for not weaning it. The mother of a syphilitic child is not infected by that child, if 'Colles's law' is correct, and at present very few exceptions to Colles's law have been observed, and some at least of these are open to doubt. For practical purposes certainly it may be taken as an invariable rule that the mother is quite safe from infection by her syphilitic infant. The other part of Colles's law must also be remembered, for it is not less important, that a syphilitic child will infect a wet nurse who is free from the disease. Under no condition is it justifiable, therefore, to run the risk of having a syphilitic infant suckled by a wet nurse.

This raises another point which is an important one in dealing with congenital syphilis, namely, the possibility or probability of infection from a syphilitic infant. If the *Spirochaete pallida* or any other organism is the specific cause of the disease, and is to be found in the superficial lesions, such as condylomata, of the inherited disease as in the acquired disease, there seems to be no *a priori* reason why the one disease should not be as easily transmitted by contagion as the other. It seems quite certain that congenital syphilis is very rarely conveyed by contagion. Dr. Coutts has brought forward facts which establish the rarity of such an occurrence beyond doubt ; but it is, I think, equally certain that the disease is contagious and has occasionally been conveyed in this way. An instance was recorded recently by Dr. W. R. Grove,[88] of St. Ives, Huntingdon, in which an infant who had had pemphigus a few days after birth, and whose mother was known to have had syphilis, developed condylomata at the anus and some sores in the mouth at the age of seventeen months. About a month later the grandmother, in whose care the infant had been left, developed two primary sores of syphilis, one on the lower lip, the other on the tonsil, and shortly afterwards showed a syphilitic rash. About the same time a daughter aged twelve years, and shortly afterwards a son aged seven years, both developed a primary sore on the tonsil, followed very soon by a syphilitic rash. The baby had been fed with a spoon, with which the grandmother and her granddaughter had tasted the food from time to time during the feeding of the infant, and it was supposed that the grandson also had used the spoon unwashed.

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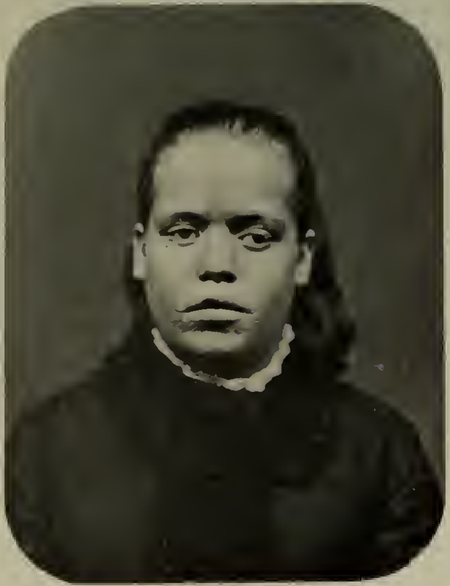
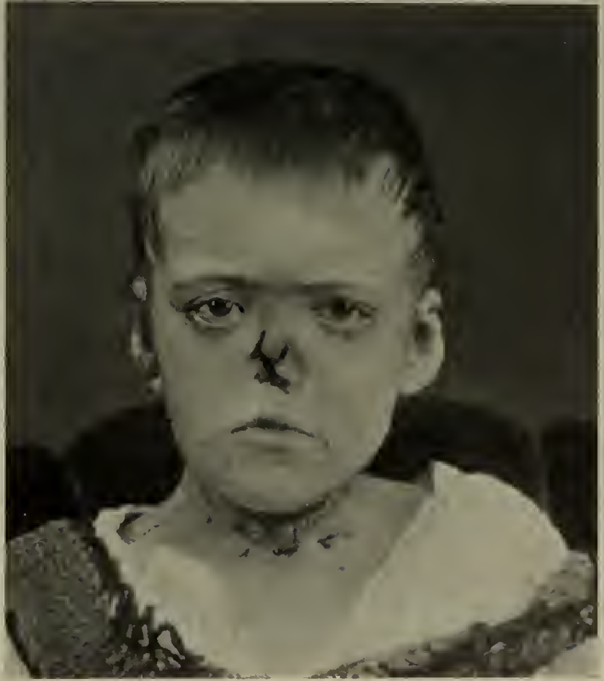
PLATE LVI



Radiating scars of the lips in congenital syphilis.
Girl aged 16 years.

From photograph kindly lent by Dr. J. Thomson.

a

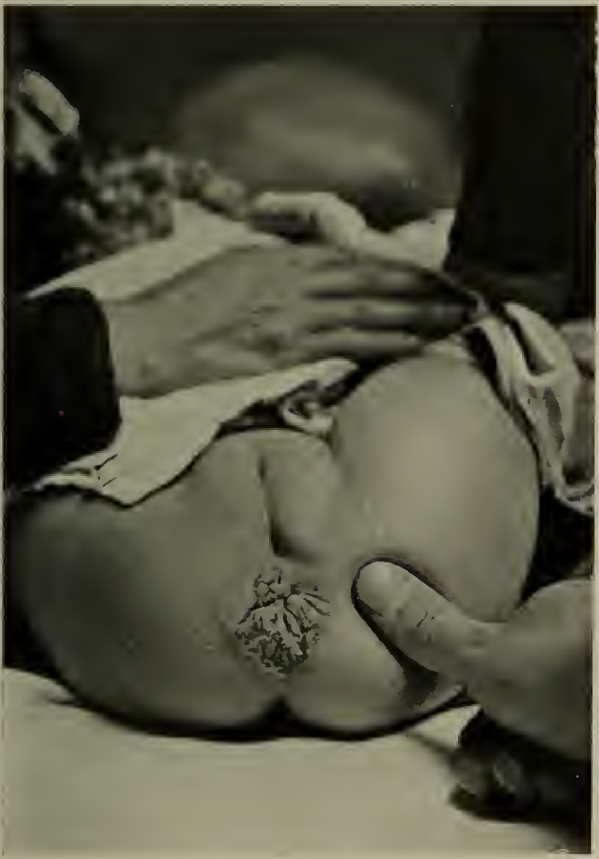


Phagedaenic ulceration of nose, ear, and neck, in girl aged
14 years with congenital syphilis.

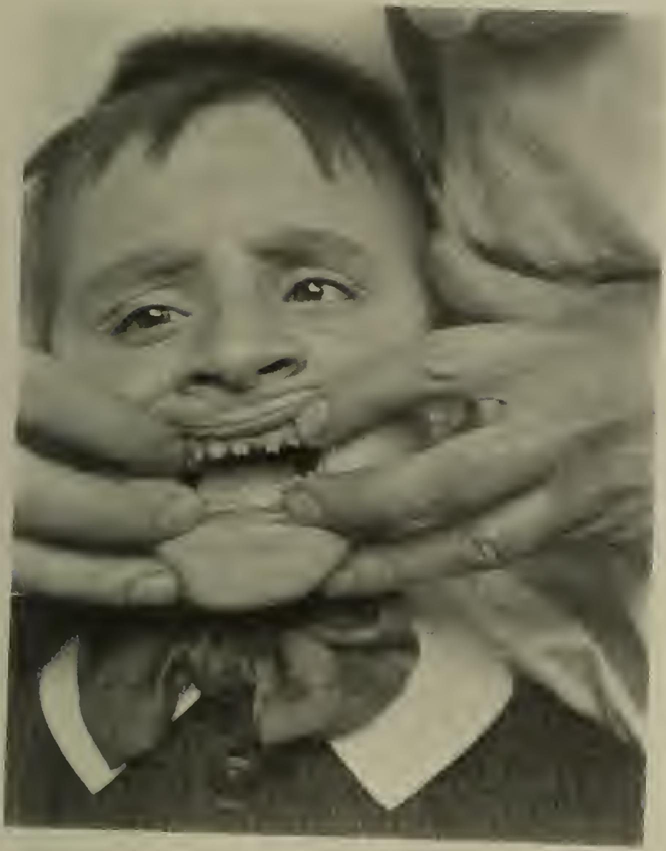
From photograph kindly lent by Dr. J. Thomson.

b

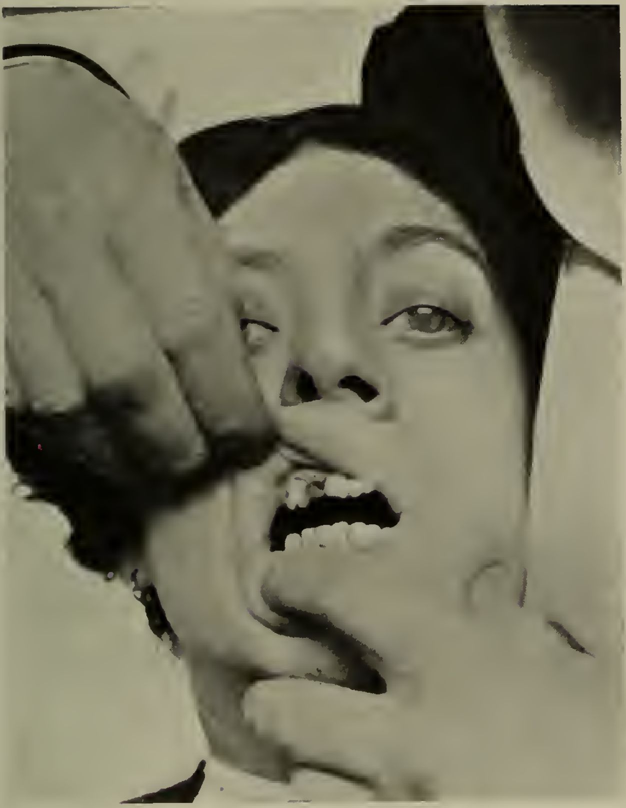
Plate LVII



Condylomatous ulceration at the anus, due to congenital syphilis. (Mr. Keogh Murphy's case.)

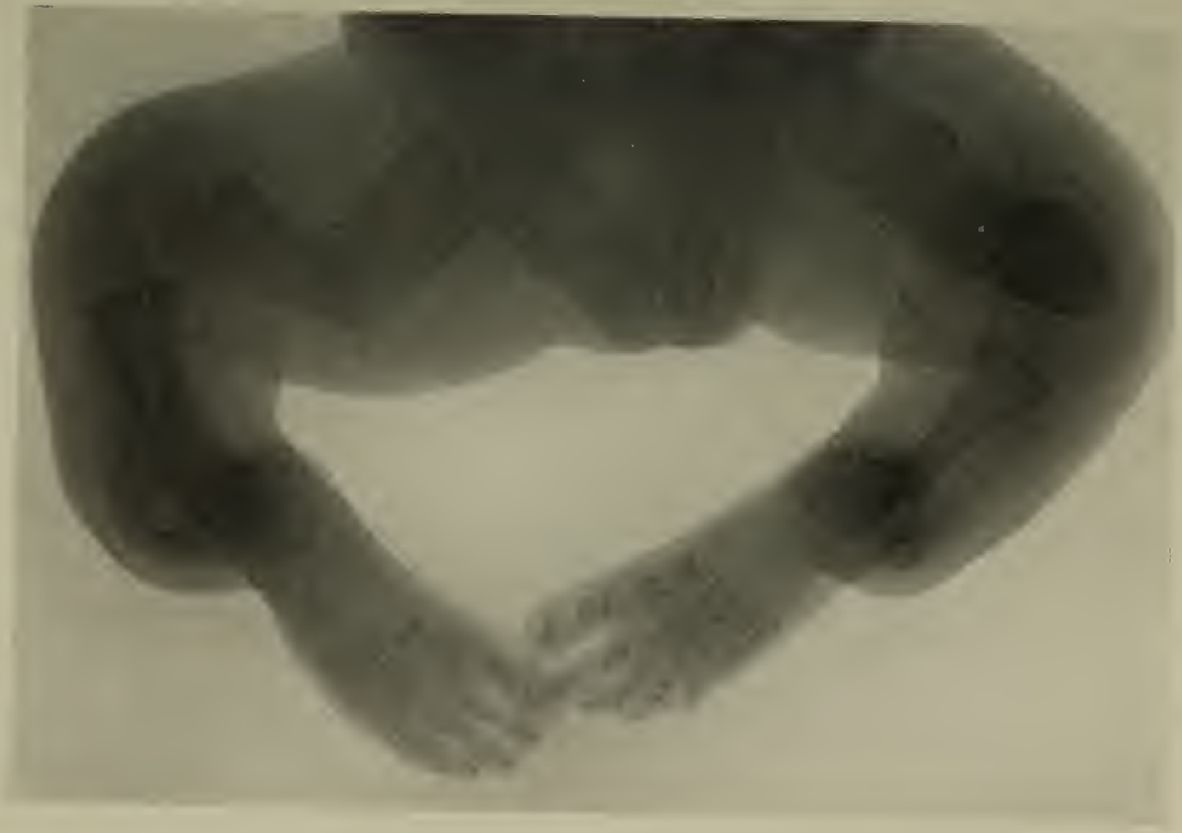


Notched upper central incisors: the photograph shows also the small, ill-developed appearance of the teeth, and their wide separation from one another, and from the lateral incisors.



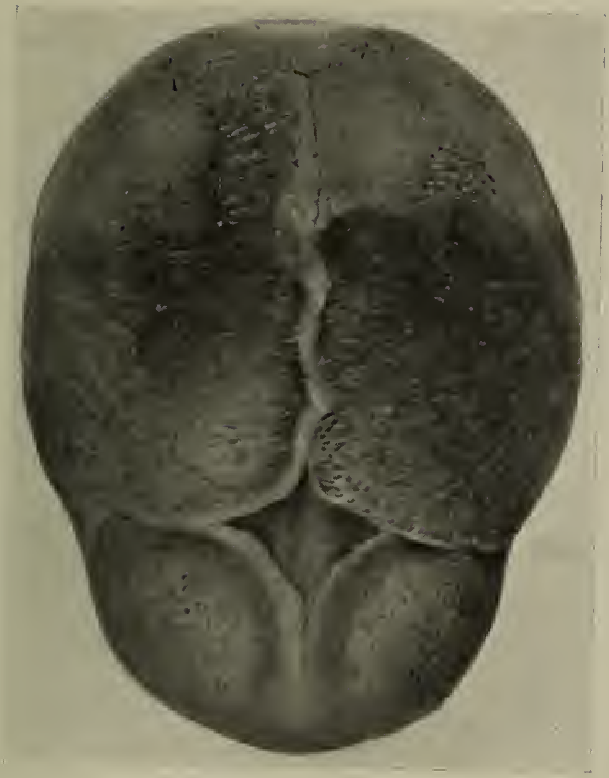
Syphilitic notching of a canine tooth, in a woman with interstitial keratitis, under the care of Mr. C. E. Wallis.

PLATE LX



Radiograph of Dr. G. A. Sutherland's case of *Osteogenesis imperfecta*, showing multiple fractures.
(Reported in *Clin. Soc. Trans.*, vol. xl, p. 264.)

PLATE LXI



Photograph of a calvaria, showing vascular thickening of the bones (Parrot's nodes).

From the Museum of St. Bartholomew's Hospital.

Plate LXII

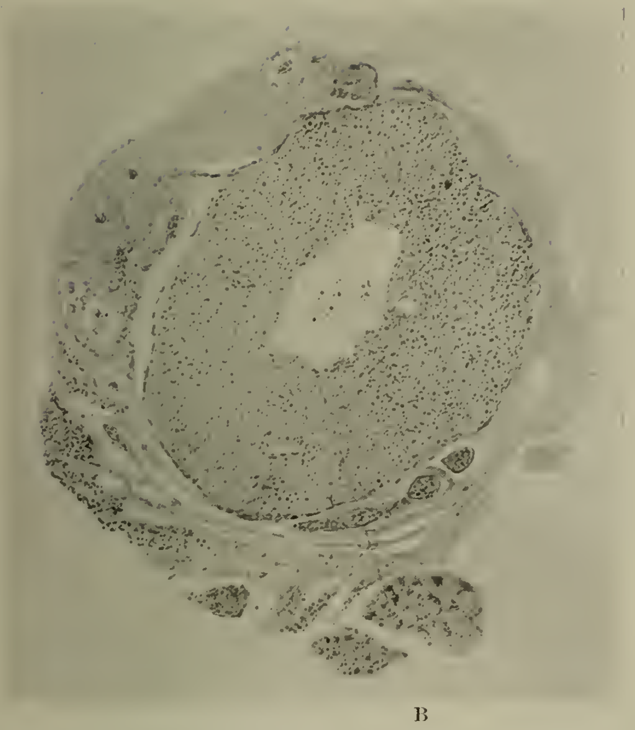


Fig. 1. Transverse section of obstructed common bile duct; the obstruction is due to syphilitic granulation tissue. From Dr. Rolleston's case, in which an interacinous pancreatitis was associated with syphilitic obstruction of the common bile duct in an infant aged three weeks.

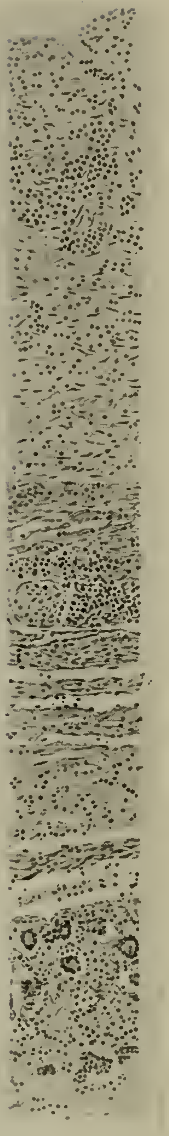


Fig. 2. Section through wall of common bile duct (along line B), showing granulation tissue mainly inside the muscular coats.

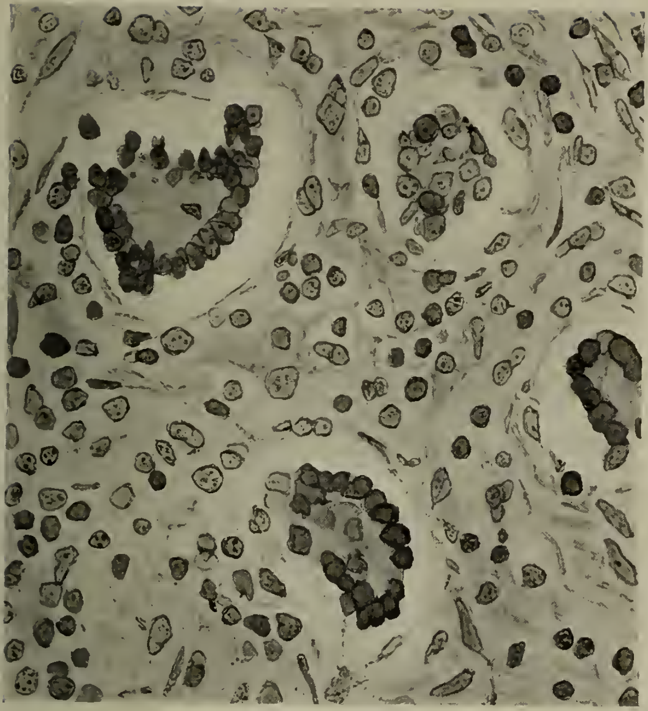


FIG. 1. Section of pancreas showing interacinous pancreatitis due to congenital syphilis. Case of Dr. H. D. Rolleston.

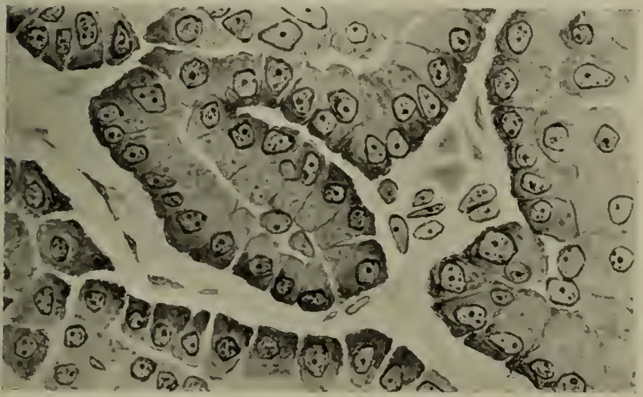


FIG. 2. Normal pancreas under same magnification for comparison.

SUMMARY OF RECENT MORE IMPORTANT ADDITIONS TO THE MICROBIOLOGY OF SYPHILIS

BY

MAJOR L. W. HARRISON, R.A.M.C.

SUMMARY OF RECENT MORE IMPORTANT ADDITIONS TO THE MICROBIOLOGY OF SYPHILIS

The following short summary of recent additions to our knowledge of the microbiology of syphilis cannot claim to be a complete *résumé* of the enormous mass of literature on the subject which has accumulated since this volume first appeared. Such a *résumé* would swell the volume to impossible dimensions, and the aim here is to include only such new matter as appears to be important from a practical point of view.

Recent advances in the treatment of syphilis have enhanced the importance of early diagnosis, and this, in turn, demands perfect familiarity with the technique of demonstrating the *Spirochaete pallida.*

For this reason special attention has been paid to this section in the following pages.

THE SPIROCHAETE PALLIDA

Description. The *Spirochaete pallida* is an extremely delicate, thread-like organism, spirally twisted and presenting several points by which it may be distinguished, with comparative ease, from other spirochaetes. The chief of these points are its extreme tenuity, the regularity and close twisting of the spirals, its weak staining affinities and its low refrangibility. In the fresh, unstained condition, it may be seen in the hanging-drop, but this demands the best optical conditions and considerable proficiency in high-power microscopy. It can be seen in the living condition much more easily by means of the dark-ground illumination, and this is the method by which it is now most frequently demonstrated.

When examined by this method it is seen to be actively motile, its movements being of four kinds: (*a*) rotation on its long axis, (*b*) bending and lashing, (*c*) contraction and extension of its spirals, and (*d*) slow progression. All of these are very characteristic of the *Spirochaete pallida*, and it will frequently betray its presence to a trained observer by its slow progression and wonderful flexibility before it has been brought properly into focus. It may bend to form an irregular circle, or an L, or, keeping the greater part of its axis straight, may form a loop of the last few microns of its length ; save *Spirochaete pertenuis*, no other spirochaete can compare with it in flexibility. On account of its slow rate of progression it is quite easy to keep the same specimen in the microscopic field for many hours together, and here again it differs from many other spirochaetes, which move more rapidly across the field. Another point of some value in the recognition of *Spirochaete pallida* is its dead-white appearance under dark-ground illumination, when viewed with an oil-immersion or a dry apochromatic objective. To appreciate this point it should be examined in the same field with such spirochaetes as *Spirochaete gracilis*, which the beginner, relying on a book description, may easily mistake for *Spirochaete pallida*. A good plan is to prepare a specimen from a chancre which is also associated with balanitis without taking any precautions to prevent the chancre exudate from becoming contaminated with the balanitic secretion. Such a specimen contains, besides *pallida*, multitudes of other spirochaetes, some of them very fine and with closely set spirals, but it will be noticed that, amongst other differences, while *pallida* is dead-white other spirochaetes are glistening. If the fine adjustment of the microscope be moved the very least amount, so as to focus on a very slightly higher level, all other spirochaetes which may be associated with *pallida* have a reddish tinge. Probably this is because *pallida* reflects all the light which strikes it, while other spirochaetes, being thicker and consequently having a surface which is less steeply curved, pass some of the rays of light and break them up. Its hair-like tenuity, the regularity, depth and close twisting of its curves, are particularly well seen in the living organism, though these characteristics are well maintained in stained specimens. Its thickness has been estimated at $\frac{1}{4}\mu$ and its length varies from 4–24 μ, being generally 7–10 μ. The width of the curves, that is, the distance from the summit of one convexity to that of the next, is very constant, 1 to 1·2 microns. This is a figure that is rarely departed from and is worth bearing in mind, as it is a point by which *pallida* may be distinguished from *Spirochaete refringens* and others which are often encountered in suspected material. In the absence of a micrometer, these curves may be measured, with approximate accuracy, by contrasting them with the diameter of a red blood corpuscle, if any happen to be in the field; remembering that the average diameter of a red cell is 7·5 microns, it will be seen that the spirochaete, in this distance, will have made from six to seven turns (Plate LXIV). In this manner the average width of the spirals can be ascertained with a fair degree of accuracy. If, however, an eye-piece micrometer is available, the value of whose divisions has been ascertained for the particular combination of lenses in use, the average measurement of the curves may be determined by taking the length of the spirochaete in microns, counting the total number of the curves and dividing the former figure by the latter.

In stained preparations the *Spirochaete pallida* characteristically maintains the regularity of its spiral formation, a point of distinction from many other spirochaetes with which it may be associated in suspected material. Irregular forms are often seen, however, in film preparations. Sometimes it appears as a delicate helical spring which has been overstrained in one portion of its length and a few of its spirals straightened out, and sometimes curved forms, loops, figures of eight, and irregularly twisted spirochaetes are seen. I have never seen such atypical forms in living preparations, and conclude that these irregularities must be produced artificially in spreading the film, or the spirochaete was engaged in one of the bending movements already described when fixed in position by the drying of the film.

The biological position of the *Spirochaete pallida* is by no means settled. If it were proved that in some stage of its life-history it assumed 'a resting form', it would strongly support its protozoal nature. Sir W. B. Leishman has shown in the case of *Spirochaete* *duttoni* that a developmental form does exist, while Balfour and O'Farrell have demonstrated by means of the dark-ground illumination that the *Spirochaete pallida* sheds highly refractile granules at some stage in its life-history, especially under the influence of salvarsan, and believe that these granules are possibly spore forms. The exact relation of the granules to the *Spirochaete pallida*, however, has not yet been demonstrated. The round spore-like chromatin bodies which Noguchi has described and figured in his cultivated spirochaetes are interesting in this connexion.

Cultivation. For some years the *Spirochaete pallida* resisted all attempts at artificial cultivation. In 1909, however, Schereschewsky claimed to have obtained impure cultures in inspissated horse serum. His observations were not confirmed at first, other observers, notably Levaditi and Stanesco, holding that Schereschewsky's spirochaetes were thicker than *pallida* and non-virulent.

In 1911 Noguchi succeeded in obtaining pure cultures with which he produced typical syphilitic lesions in rabbits. He first obtained an impure culture by inoculating, with syphilitic rabbit's testis, serum water (sheep, horse, or rabbit serum 1, distilled water 3), to which was added a small piece of fresh sterile rabbit kidney or testis. The advantage of using syphilitic rabbit's testis consists in its being almost free from other organisms and very rich in spirochaetes. The culture was incubated at 37° C. under very strictly anaerobic conditions. The resulting impure culture of *Spirochaete pallida* was freed from associated bacteria by taking advantage of the facts that *Spirochaete pallida* will grow through a Berkefeld filter more quickly than other organisms and will also penetrate further into the surrounding culture medium. After becoming accustomed to artificial conditions, the spirochaetes were induced to grow in serum agar to which a piece of sterile rabbit's kidney or testis had been added.

Subsequently Noguchi obtained cultures directly from human lesions by inoculating deep ascitic or hydrocele agar stabs (2 per cent. slightly alkaline agar, 2 ; ascitic fluid, 1 ; total in tube, 15 c.c.), at the bottom of which was placed a piece of sterile rabbit's tissue. The material for inoculation is received into sterile saline in 1 per cent. citrate of soda and cut into small pieces. One of these is pushed to the bottom of each tube, while into the same tube are forced several drops of an emulsion of the syphilitic material. Some sterile liquid paraffin is poured on the top of the medium, and the tubes are incubated at 37° C. under strictly anaerobic conditions. After two to three weeks the now putrefactive culture is examined by dark-ground illumination, and if *Spirochaete pallida* is found some of the growth is carried to the bottom of more ascitic agar stabs by means of a capillary pipette, taking care not to split the medium. After two or three weeks *Spirochaete pallida* is found to have grown out into the medium as a faint hazy growth. The upper surface of the column of medium is sterilized with sublimate alcohol which is poured away, and the tube is broken at its middle with a diamond and the application of a red-hot glass rod. The upper half of the tube is removed, leaving the cylinder of medium standing up. The surface of this is sterilized and the cylinder gently broken across so as to expose some of the hazy growth. A little of this is picked up with a capillary pipette and inoculated into a number of other stabs ; by repeating the process two or three times other micro-organisms are gradually left behind. By a very ingenious but simple method [1] the culture is induced to grow in a fluid medium.

With his cultures Noguchi claims to have produced typical syphilitic lesions in rabbits and monkeys. His ‘ luetin ’, prepared from cultures of *Sp. pallida*, when injected into the cutis vera produces in some syphilitic patients skin lesions which are analogous to the reaction obtained in tubercular subjects by the similar use of tuberculin, and animals which have been inoculated with cultures of human *pallida* develop in their blood-serum substances which have the property of binding complement when incubated with antigen prepared from syphilitic rabbit's testis.

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[1] H. Noguchi, ‘ A Method for cultivating *T. pallidum* in fluid media,’ *Journal of Experimental Medicine*, vol. xvi, 1912.

Levaditi and Danulesco do not believe that Noguchi's spirochaetes are *pallida*, because they have been unable to grow *Sp. pallida* by his method, and in one of Noguchi's own cultures which they received the spirochaetes were not typical, conforming more to the characteristics of *Sp. gracilis*, besides being non-pathogenic for animals. These objections do not appear very valid, since, as Noguchi previously pointed out, pallida will change its morphological characters under adverse conditions of culture, and it is also quite easy to imagine that such a micro-organism could easily become non-pathogenic under artificial conditions.

Other workers, notably Sowade, Schereschewsky, Hoffmann, and Nakano, claim to have obtained pure cultures by methods which are rather simpler than those of Noguchi. Briefly, these workers first obtain impure cultures by inoculating with pieces of syphilitic papule, chancre, or condyloma, horse serum which has been sterilized by heating at 58° C. for four hours on each of four days and then made gelatinous by raising its temperature very gradually to 65° C. or 70° C. To isolate the spirochaete from banal organisms Nakano inoculates with the impure culture inspissated horse serum contained in a small Reichel filter, which, in turn, is surrounded by inspissated horse serum. The spirochaetes are the first micro-organisms to grow through the filter, and subcultures are made as soon as the growth appears in the medium outside. Sowade and Schereschewsky depend on the fact already mentioned that *Sp. pallida* grows faster into the surrounding medium than other organisms. The medium becomes liquefied around the contaminating organisms, but beyond this, in the solid medium, is the milky-white growth of *Sp. pallida.* When liquefaction has well advanced (about the fourth day) 70 per cent. alcohol is run along the canal of inoculation to the syphilitic material. This destroys the banal organisms. After ten minutes the alcohol is replaced by sterile distilled water and this again by sterile paraffin oil. The *Spirochaete pallida* having grown into the medium beyond the area of liquefaction is not touched by the alcohol. To make subcultures the outside of the tube is carefully sterilized and it is then broken across below the upper level of the growth. The medium is cut across with a sterile knife. A specimen is taken from the situation of the growth and examined under darkground illumination. If found to be swarming with spirochaetes the subculture is made. One or two subcultures may have to be made before cultures are obtained which are free from other organisms.

Animal Experiments. More recently the scrotum and testis of rabbits have been used for inoculation experiments and have proved more convenient. A piece of syphilitic tissue, chancre, or condyloma or a thick emulsion of a culture of *Sp. pallida,* is introduced either into the testis or under the skin of the scrotum. The resulting lesion, either a nodule in the skin, which may ulcerate, or a spreading infiltration, or orchitis, generally commences within six weeks, but when the disease is passed from one rabbit to another by successive inoculations the virus gradually increases in virulence and the incubation eventually becomes as short as two weeks. Recently Sowade claims to have induced constitutional syphilis in rabbits, loss of hair and weight, papular and ulcerating skin lesions, paronychia and iritis by means of intravascular injections of artificially cultivated *Sp. pallida.*

Some of Noguchi's experiments with pallida cultures have already been mentioned (p. 375), but probably the most important are this worker's experiments in connexion with general paralysis of the insane. By inoculating the testes of rabbits with pieces from the brains of general paralytics he succeeded, after some failures, in producing syphilitic orchitis. The incubation period of these lesions was considerably longer than that of similar lesions produced by inoculating with syphilitic virus from such sources as skin and mucous membrane lesions, and it seems as if the virus derived from the brains of general paretics has low virulence for rabbits. It may be mentioned here that Nichols and Hough have produced keratitis in rabbits by inoculating them with brain of general paretics. Noguchi's experiments, which were designed to produce general paralysis in rabbits, are most interesting, and may throw a valuable light on the aetiology of so-called parasyphilitic lesions. Finding that rabbits are particularly resistant to intra-cerebral inoculation with syphilitic virus, he produced in a series of eight rabbits a hypersensitive condition of the tissues to *Sp. pallida* by repeated intravenous injections of these micro-organisms, the injections being carried out at intervals of five days for five months. After allowing another five months to elapse he introduced minute particles of syphilitic virus into the brain of each of the eight sensitized rabbits and at the same time inoculated in a similar manner four other rabbits which had not been prepared in any way. At the end of two months the eight sensitized rabbits began to be stupid and inactive, suffered slight spasticity of the legs, and became slightly ataxic. These symptoms gradually increased in intensity for a period of three months, after which the animals were gradually killed off and their brains examined. In one brain spirochaetes were found and in all there was proliferation of endothelium and perivascular infiltration, with proliferation of neuroglia in a few. In the majority of cases the brain-cells remained intact. The four (control) rabbits which had received no sensitizing preparation remained well.

Infection. Animal experiments have done much to increase our knowledge of the pathogenicity of the *Sp. pallida* under different conditions. As might be expected, lesions which contain the spirochaetes in greatest numbers are those which are the most successful sources of inoculation and may therefore be considered to be the most dangerous from the point of view of accidental infection. Thus the primary sore, condylomata, mucous patches, and the skin and mucous membrane lesions of congenital syphilis have been shown in this way to be particularly dangerous, though it must be remembered that tertiary lesions, in which it is particularly difficult to find spirochaetes, have been successfully used in inoculation experiments.

After removal from the body the *Sp. pallida* quickly loses its virulence and dies. Opinions differ as to the length of time it can remain alive after removal from the body. Levaditi believes that death occurs in 6–8 hours ; Beer claims to have kept it alive under anaerobic conditions for 33 days, but this does not seem to be of practical interest from the point of view of accidental infection. In specimens prepared for dark-ground illumination I have occasionally seen independent movement up to two days, but not longer. It is killed at once by drying, with weak antiseptics, and by a temperature of 51° C.

The conditions under which the *Sp. pallida* is most successfully planted on a fresh host are of considerable practical interest. Animal experiments have shown that infection most frequently follows when the virus is planted on or in the true skin. A minute abrasion, not sufficient to draw blood, but enough to cause a slight oozing of serum, is the site on which the parasite can best become accustomed to its new surroundings. Finger and Landsteiner and Pinard succeeded in producing infection under peculiarly difficult conditions, to be mentioned later, by pushing the virus in large amounts into pockets under the epidermis or in the *cutis vera*.

Though these sites are the best for experimental inoculation, it must be remembered that even the lower animals have been successfully inoculated by intravenous injections, injections into the testis, and even subcutaneously, so that it is not absolutely necessary that the spirochaete be planted in the skin or mucous membrane for infection to follow. If this is the case with lower animals, which we know are much less susceptible to syphilis than man, it is not surprising that it should occur in man. The undoubted cases in which syphilis has followed an accidental puncture with an infected needle, without the development of a primary sore, are examples of this.

Incubation. As is well known in the case of man, and has been shown by animal experiments, a period of apparent quiescence follows inoculation before the primary sore begins to appear. In man this period is generally about thirty days. It is not quite clear why such a period should elapse before the tissues react sufficiently to show macroscopic changes. It is certainly not because the spirochaete remains entirely inactive during this period, since Levaditi and Yamanouchi have shown that microscopical changes commence very early. These workers believe that the slight reactive changes caused by the presence of the spirochaete in the tissues produce increased nourishment for the parasites, which rapidly multiply in the site of inoculation when the nourishing substances have accumulated in sufficient amount.

It might reasonably be supposed that as the incubation period is so long it would be possible to prevent syphilis by excising the site of inoculation at an early date. Unfortunately this is not the case. Neisser found by animal experiments that infection followed the inoculation if excision was delayed for twelve hours. Metchnikoff showed that calomel ointment (30 per cent.) rubbed into the site of an experimental inoculation an hour after it had been carried out prevented infection in the case of a medical student and also of a macaque ; but a macaque which was energetically rubbed with the same ointment twenty hours after inoculation developed a chancre. Neisser has infected animals with the blood of monkeys on the fifth day after their inoculation and with the spleen on the twelfth day.

It is evident, therefore, that very soon after inoculation the parasite spreads quickly into the general circulation. It appears to do so chiefly by way of the lymph-vessels, but there is reason to believe that it also travels, more directly, by the blood-vessels.

After the development of the primary sore another period of apparent quiescence follows, and Neisser has shown that during this period, which precedes the so-called secondary stage, the chief sites of the parasite are the bone marrow, spleen, and testis. Before these experiments and the advent of the Wassermann test it was believed that the disease was quite latent between the clinically primary and secondary stages, but the Wassermann test now also shows that although no clinical signs are apparent, the spirochaete is by no means inactive, and the same applies to the so-called latent period which succeeds the secondary stage.

It is necessary to emphasize this, since there is too great a tendency to consider that syphilis is latent when clinical signs are absent.

Distribution of the Spirochaetes in Syphilitic Lesions. In view of the long-debated question of the relation of syphilis to general paralysis, great interest attaches to the discovery by Noguchi and Moore of *Spirochaete pallida* in the brains of twelve out of seventy paretics. The observations of these workers have since been confirmed by others, and Noguchi has now found the parasite of syphilis in the brains of 48 out of 200 general paralytics. The method employed by Noguchi and Moore for most of their cases was a modification of Levaditi's which is described later, but in addition to this Noguchi examined by means of dark-ground illumination emulsified material from six fresh paretic brains and found *Sp. pallida* in one. Marie, Levaditi, and Bankowsky were successful in finding *Sp. pallida* in 3 out of 14 paretic brains prepared by the silver method and in 6 out of 6 fresh brains material from which was examined by dark-ground illumination, while Forster and Tomaczewski, by puncturing the brains of general paralytics during life and examination of the material by dark-ground illumination, found the same micro-organism in 2 out of 4 cases.

As to the distribution of the parasites, Noguchi found them in greater numbers in the cortical layers than in the white matter. They were found sometimes in groups of varying size, sometimes singly, scattered irregularly amongst the nerve cells and neuroglia. The spirochaetes were more intimately related to the nerve cells and their processes than to the vessels. In some cases part of the spirochaete was found lying within the cytoplasm of a nerve cell and sometimes they were found in the spaces round the axis-cylinder processes. *Sp. pallida* was very rarely found in the vicinity of the vessels and practically never within them, nor was it found in the pia mater. Noguchi has also found *Sp. pallida* in a posterior column of one out of twelve cases of tabes dorsalis. His animal experiments in connexion with so-called parasyphilis have been described. The importance of this work is obvious and it seems reasonable to predict an early revision of the term 'parasyphilis'.

Demonstration of the Spirochaete Pallida and its differentiation from other Spirochaetes

The *Spirochaete pallida* can be demonstrated in serum expressed or aspirated from syphilitic lesions, or in sections of infected tissues after removal of the latter from the body.

In serum from syphilitic lesions it may be examined fresh by means of the dark-ground illumination, or in films. In the latter case the exudate is mixed with some preparation such as Chinese ink, which will stain the background without touching the spirochaetes, or the film is stained so as to dye the parasite.

Of all methods examination by dark-ground illumination is undoubtedly the most convenient, rapid, and certain. This is so much the case that since the perfection of this method the *Spirochaete pallida* from being one of the most difficult organisms to demonstrate has become one of the very easiest.

The value of a routine microscopic examination of the serum from any suspected early syphilitic lesion cannot be too strongly emphasized. It affords a practicable means of diagnosing syphilis long before the clinical signs are clear or the Wassermann reaction has become positive, and in secondary lesions a diagnosis can frequently be made by a microscopic examination without recourse to the Wassermann test, which even in this stage may occasionally be negative, and in any case entails delay and a more complicated procedure. In illustration I may mention that I have demonstrated *pallida* in many chancres no larger than a pin's head, in a chancre on the inferior concha bone, in secondary skin lesions when the Wassermann reaction was negative, and in all varieties of secondary mouth and throat affections.

In pre-salvarsan days the early diagnosis and treatment of syphilis were considered of great importance. They are infinitely more so now that salvarsan has been introduced, since the experience of all who have used this remedy shows that the great opportunity of curing the disease rapidly is in the very early stage before the sore has become indurated, the glands enlarged, or the Wassermann reaction positive ; *in fact, in the stage when nobody would venture to diagnose syphilis on clinical grounds.*

The surgeon who would give his primary case the best chance should think first, therefore, not of induration, nor of glands, nor even of a blood-test, but of microscopic examination of the exudate from the sore for *Spirochaete pallida*, and should lose no time in carrying this out or having the examination made for him.

Whichever method of demonstrating the spirochaete is chosen the manner of collecting the serum exudate is the same and may be considered first.

The general principles are to obtain serum from below the surface and to avoid as far as possible contamination with surface organisms, and too great admixture with blood cells. Surface organisms often include other spirochaetes, which may be very fine and tightly rolled and are apt to confuse the beginner. Blood cells obscure film preparations and in fresh specimens may reflect too much light into the field.

The lesion (chancre, condyloma, papule, mucous patch, &c.) should first be cleaned, by rubbing it over with wool or gauze soaked in saline, and then dried. In dealing with a chancre which is within a tight prepuce it may be difficult to keep the surface of the sore clean on account of pus welling out from behind the prepuce. In such cases it is well to pack in some dry cotton-wool behind the sore so as to isolate it. The specimen should be obtained from the margin of the lesion, especially if it is ulcerated. This may be lightly scratched with the edge of a scarifier so as to remove the superficial epithelium without, if possible, drawing blood; or rubbed over with spirit, which is then dried off; or the point of a capillary pipette may be run in below the surface and the serum drawn out by means of a rubber teat. Of these I usually employ the scarifier.

In some situations, e. g. on the fauces or within the nose, it may not be possible to reach the sore by any of these means, and I have found the following plan very successful. A capillary pipette is cut off square to a convenient length; the open capillary mouth of the pipette is then rubbed lightly over the surface of the lesion and as this becomes abraded the blood and serum which exudes flows along the pipette; a very small drop is all that is required. Sometimes, as in the case of a secondary rash, it may be difficult to induce serum to exude. Here, if practicable, a blister may be applied and the blister fluid examined, but generally it is only necessary to apply some form of suction after scarifying the surface. The simplest way of doing this is to smear the mouth of an ordinary test-tube with vaseline, heat the blind end of the tube in a flame, and then apply the test-tube so that its mouth encircles the scarified area; the test-tube acts, of course, just like a cupping glass. If from any of these procedures blood flows too freely it should be gently soaked up with a little wool or gauze, and the operator should wait for a few minutes till the blood clots. The best specimens are made with clear serum, and at most the serum should be light pink.

To obtain serum from a gland, having sterilized the overlying skin, the gland is picked up with a finger and thumb, and the needle of an all-glass hypodermic syringe run into its substance. The needle-point is worked about a little within the gland and suction then applied with the piston of the syringe. The needle is withdrawn, and the aspirated material, which may fill only the needle, forced out into a watch-glass, where it can be emulsified with a little saline or distilled water according to the method of examination to be employed.

The further procedure will be described under each of the methods of microscopic examination, but it may be mentioned here that if the operator wishes to send the specimen to a laboratory for examination, it is by far the best plan to allow the serum to run into a capillary tube, shake the column of fluid down till it is about an inch from the capillary mouth, and then seal off with a fine flame above and below the specimen. This gives the pathologist full choice of methods of examination.

Dark-ground illumination. This method of examination was invented many years ago, but until quite recently was only suitable for low-power objectives, and was not greatly employed in bacteriological technique. The difficulty of seeing the *Spirochaete pallida* under axial illumination, such as is used for ordinary hanging-drop specimens, led to the introduction of the present perfected apparatus into the bacteriological laboratory.

A microscope which is fitted for dark-ground illumination is sometimes called an ultra-microscope, a term which seems unfortunate, since it is inappropriate and also conveys the idea that a dark-ground apparatus means a microscope which is specially built for the purpose, and not, as it does, simply an ordinary bacteriological microscope with one or two accessories for use when required.

Of these accessories the chief is a special condenser which is fitted in place of the ordinary sub-stage condenser. The object of this condenser is to direct the rays of light from the mirror of the microscope so that they strike solid objects in the specimen at a very oblique angle, as is illustrated in the accompanying photograph (Fig. 1), which shows the path of rays from a Leitz concentric condenser. In this it will be seen that the rays come to a very sharp focus and diverge again at a wide angle. If, in place of the condenser usually supplied, the microscope is fitted with a spherically and chromatically corrected oil-immersion condenser of N.A. 1·4, efficient dark-ground illumination can be obtained by placing a central stop on the diaphragm carrier. Such an arrangement costs no less than the usual one of having the ordinary type of condenser for stained specimens and another, special, condenser for dark-ground work, but it has the advantage that for ordinary work a better condenser is used and for dark-ground the change in the sub-stage illumination can be made instantly.

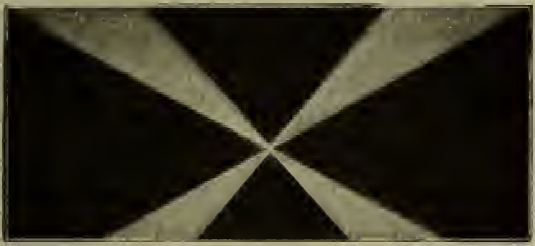

FIG. 1. Photograph of rays of light leaving a Leitz dark-ground condenser.

The mechanism of the two main forms of special dark-ground condenser will be understood from a study of Figs. 2 and 3, and it is only necessary here to describe generally the path of rays after leaving the condenser in order that the directions for using it may be understood.

Leaving the upper surface of the condenser, the rays pass unrefracted to their focus on the upper surface of the microscope slide. For this two conditions are essential: (1) a film of cedar-wood oil or distilled water must be interposed between the slide and the condenser, and (2) the slide must be of the thickness, or at any rate no thicker than that, which is suitable for the particular make of condenser in use; otherwise the focus would fall within the substance of the slide. Reaching the upper surface of the slide, where they are focussed, those rays which meet no solid object pass on to the coverslip, and their further course is determined by the medium which is above the coverslip. If this is air, as when a dry objective is being used, they are reflected from the upper surface of the coverslip and lost; if the medium above the coverslip is oil, as when an oil-immersion objective is employed, the rays pass on but are not taken up by the objective

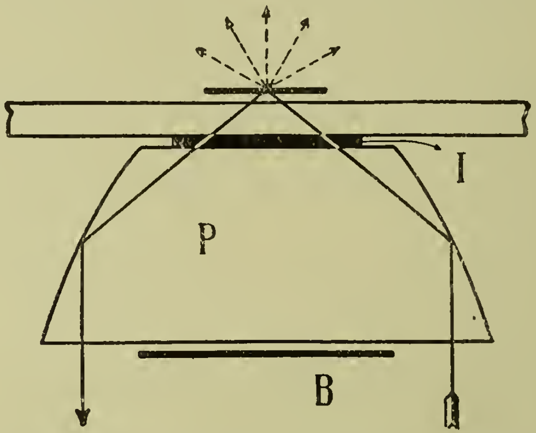

Fig. 2. Mechanism of Zeiss dark-ground condenser. *P*, plano-convex body of glass, the convex surface being formed by a paraboloid of rotation; *B*, central stop to cut off central rays from mirror; *I*, immersion fluid between condenser and microscope slide.

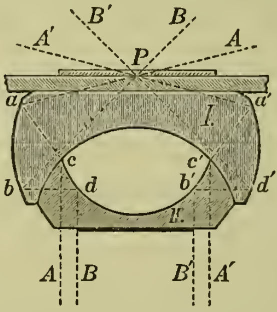

Fig. 3. To illustrate path of rays in Leitz dark-ground condenser. Lower *A B B′ A′*, rays from the mirror; *c d b′ c′*, points where rays from the mirror are first reflected; *a b a′ d′*, points where rays are next reflected; *P*, focus of rays on upper surface of slide; upper *A′ B′ B A*, final course of rays when medium above coverslip is homogeneous with glass (cedar-wood oil).

provided that the numerical aperture of this is less than 1. In either case the result is darkness, and this constitutes the dark background. As the numerical aperture of all oil-immersion lenses is more than 1, when such an objective is used it is necessary to stop it down. This is done by means of an inexpensive device, which is the second accessory required to convert an ordinary microscope to a dark-ground apparatus. Those rays of light which meet solid objects (spirochaetes, blood cells, bacteria, &c.) in the specimen are deflected upwards by these, and, entering the microscope, are seen in the image which is viewed with the eyepiece. Thus the picture of bright objects on a dark background is produced.

There is only one further point to mention before passing on to the technique of mounting the specimen for examination. If the rays of light passing through the film of oil or water which is interposed between the slide and condenser meet an air-bubble, however minute, they are deflected upwards and, passing almost vertically through the specimen, illuminate the whole field, destroying the background. Consequently it is necessary to avoid the inclusion of bubbles in this film.

The following directions will be found applicable to the mounting and examination of most specimens: (1) Transfer the drop of serum to a thin coverslip by touching it with the latter held in a pair of Cornet forceps, or by forcing the serum from a capillary tube on to the coverslip. The latter operation is most safely done by breaking one end of the capillary tube and holding the the other in a flame; the expanding hot air drives the serum before it out of the tube. If the drop is too minute to fill the space between slide and coverslip, or if it contains much blood, a drop of 0·5 per cent. salt solution should be added.

(2) Turn the coverslip over and drop it gently on a slide of the correct thickness (as recommended by the maker of the dark-ground condenser in use), so as to form a film which is as free from air-bubbles as possible between the slide and coverslip.

(3) Make the film as thin as possible (so as to bring the solid objects in the specimen close to the surface of the slide) in the

following way : Fold a piece of lint or filter paper into a number of thicknesses and spread it out on the thigh ; then turn the slide over and press it very firmly, with the coverslip down, on the absorbent surface.

(4) Ring the coverslip with vaseline.

(5) Arrange the light with relation to the microscope so as to get the best possible illumination of the mirror. The source of illumination may be chosen from a number of sources, of which the following may be mentioned : sunlight ; electric, arc or Nernst ; incandescent mantle, coal gas, spirit vapour, or petrol vapour ; and paraffin oil. Generally speaking, especially when using the Leitz pattern of condenser, which requires a less intense source of illumination, it is not necessary to employ a bull's-eye condenser when using arc or Nernst lamps, and the Leitz pattern condenser gives an excellent image without a bull's-eye with an ordinary inverted gas mantle when the concave mirror is used. Assuming that a bull's-eye condenser is being used, arrange this about ten inches from the plane mirror of the microscope and place the light behind it so as to throw an image of the illuminant on the plane mirror. This can be judged by holding a piece of white paper over the mirror. The light should fill the mirror as completely as possible.

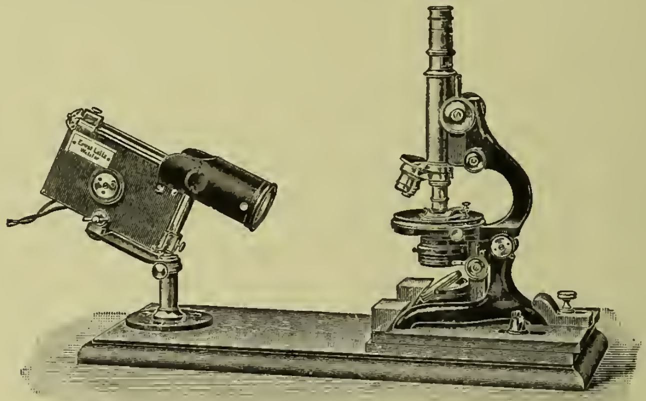

Fig. 4. To illustrate a convenient arrangement of microscope and lamp for dark-ground illumination. The lamp is a Lilliput arc, with bull's-eye set at correct distance in the sleeve.

It may be necessary to centre the dark-ground condenser. The Zeiss condenser should be central when slipped into its sleeve, but other patterns, notably the Leitz, need centring. To do this, rack up the condenser till it is flush with the microscope stage and view its upper surface through a low-power objective (two-thirds) and a low eyepiece (No. 2), bringing the two concentric rings engraved on its upper surface into focus. If the rings cannot be seen, the top of the condenser should be cleaned with xylol. By means of the centring screws bring the rings into the centre of the field.

(6) Place a drop of distilled water, or cedar-wood oil, on the top of the condenser and another on the under surface of the slide opposite the coverslip. Turn the slide over and, having racked down the condenser slightly, place the slide on the microscope stage, coverslip up, so that the drop overhangs the condenser. Rack up the latter till it is flush with the stage. The two drops coalesce, and here, as already mentioned, it is necessary to see that no air-bubble has been imprisoned between the slide and condenser.

(7) If the light has been correctly arranged, with a little manipulation of the mirror a light area should be apparent in the middle of the coverslip. It is useless attempting to view the specimen till this area has been obtained.

(8) Adjust the condenser finally so as to obtain the best possible focus. To do this, view the specimen with the low-power objective, &c., used for centring, and a bright area will be seen in the centre of the field when the preparation is in focus. With the objects in the specimen in focus, rack the condenser slightly up or down so as to reduce this spot to its smallest dimensions. If the bright area is not in the centre of the field, manipulate the mirror so as to bring it central.

(9) The specimen may now be viewed with a higher power objective ($\frac{1}{12}$ in. oil-immersion, with No. 4 or 8 eyepiece, 4 mm. apochromatic, or $\frac{1}{6}$ in. with a No. 8 or 18 eyepiece). Generally speaking, the higher the eyepiece the more powerful should be the source of illumination. With a $\frac{1}{6}$ in. or a 4 mm. apochromatic objective and a No. 8 eyepiece the specimen can rapidly be viewed,

and it is not necessary to employ high magnifications for diagnostic work.

Film preparations—Burri's method. The principle of this is that Chinese ink will become incorporated with the medium in which spirochaetes, blood cells, &c., are suspended, but will not penetrate these. Consequently, when a drop of syphilitic exudate is mixed with a drop of Chinese ink and the mixture spread like a blood film, the background is stained black but spirochaetes appear as white spirals. Briefly, it is another method of obtaining a dark background. The best ink for the purpose is Günther-Wagner's waterproof Chinese ink, and to make it homogeneous it should be well centrifugalized before use, or, as Captain A. T. Frost recommends, mixed with tincture of iodine in the proportion of 1 of iodine to 600 of ink. A drop of the prepared ink and one of the suspected exudate are mixed together at one end of a microscope slide, and with the end of another slide a thin film is spread. When dry the film is examined with an oil-immersion lens. The spirochaetes appear as white spirals on a granular black background. Opinions differ as to the reliability of this method of demonstrating the *Spirochaete pallida.* While some maintain that it is absolutely reliable for diagnostic purposes, others hold that by this method other spirochaetes may be made to appear like *Spirochaete pallida.* McIntosh and Fildes object that in a thinly spread film *Spirochaete pallida* may appear abnormally thick and in a thick film other spirochaetes may appear abnormally fine ; that great distortion occurs and that the most important differential sign, that of motility, is lost. In the writer's experience the greatest objection is the loss of motility, with the knowledge that very fine spirochaetes are often seen in living specimens which are chiefly distinguished from *Spirochaete pallida* by the character of their movements. At the same time one must admit that so far in examining specimens containing only these very fine spirochaetes, but not *Spirochaete pallida*, both by dark-ground illumination and by the Burri method, it has been easy to exclude *Spirochaete pallida* in the Burri specimen on account of the fact that when spread in films the other spirochaetes have lost much of their corkscrew formation. The writer, however, prefers the dark-ground illumination method of diagnosing *Spirochaete pallida*, as being free from any objection and more rapid.

As a substitute for Chinese ink, and one which at once gives a more homogeneous field than ink, I have found that a suspension of collargol has many advantages. The suspension is made up according to the directions of the makers (Chemische Fabrik von Heyden), one part of the powder being placed in a black bottle (or an ordinary bottle covered with black paper) and nineteen parts of distilled water poured on it. After standing for a few minutes the bottle is well shaken and again allowed to stand. A few minutes later the bottle is again shaken and the suspension is then ready for use. It is used exactly in the same way as Chinese ink, and on examination the spirochaetes appear as white spirals on a reddish-brown background which is almost perfectly homogeneous. This modification requires a light which is rather stronger than that which is necessary for the Chinese ink specimen, but good daylight is quite sufficient.

Eisenberg (*Centralbl. f. Bakt.*, Beilage zu Bd. liv.) recommends the following substitute for Chinese ink :

Saturated solution of China blue . . .	3
Saturated solution of cyanosin . . .	1

Mix two days before use and steam in sterilizer.

Staining of Film Preparations. It is necessary to observe certain precautions in preparing the film if the best, or indeed if any, results are to be expected. The slide or cover-glass, on which the film is to be made, must be perfectly clean and free from grease ; any of the methods recommended for the preparation of slides for flagellar staining will answer the purpose, but perhaps the simplest is to pass the slide thirty or forty times through the flame of a Bunsen burner. Next in importance, the film must be as thin as it is possible to make it. The material may be lightly rubbed over the surface of the slide, or, if of fluid consistency, it may be spread by any of the means employed in the preparation of blood films. If, in either instance, the film is too thick, failure is sure to result, since the spirochaetes will only take the stain when lying in a thin layer of the surrounding medium; again, if the material is thickly spread, the formation of deposit is favoured, and, if this occurs, there is little hope of being able to recognize them.

Fontana has introduced a stain which acts rapidly and is very successful. As modified by Tribondeau (*Bull. de la Soc. de Dermatol. et de Syphilogr.*, November 1912), it is prepared and used as follows :—

A thin film of the secretion, as free from blood as possible, is spread on a slide and allowed to dry. It is covered repeatedly for about a minute with the following (Huge's) solution :

Pure acetic acid	1
Formalin, 40 %	2
Distilled water	100

To complete fixation alcohol is dropped on the slide and then flamed.

The following mordant is then applied :

Tannic acid	5
Distilled water	100

warming gently till steam rises and then allowing to act for 30 seconds longer.

The specimen is washed under the tap for a few seconds, the excess water thrown off, and the slide then covered with Fontana's solution, which is prepared as follows : To a 5 per cent. solution of silver nitrate ammonia is added drop by drop with a capillary pipette till a sepia precipitate forms and then disappears completely. To this solution is added more 5 per cent. silver nitrate solution till a solution is produced which remains slightly cloudy on shaking. The slide covered with this solution is warmed gently till steam arises and the solution is then allowed to act for 30 seconds longer.

Spirochaetes appear dark brown to black and are easier to find than in specimens stained by other methods. They appear, on the whole, rather thicker. The specimen fades in a few days under cedar oil or Canada balsam.

Staining of sections. Noguchi (*Journ. Cut. Dis.*, August 1913) recommends the following modification of Levaditi's method for the detection of *Sp. pallida* in brain and spinal cord. The piece of tissue is hardened in 10% formalin and a slice of it, 5–7 mm. thick, is put into a mixture of formalin 10, pyridin 10, acetone 25, alcohol 25, and distilled water 30 for five days at room temperature. After washing thoroughly in distilled water for 24 hours it is placed in 96 % alcohol for three days and again washed in distilled water for 24 hours. It is then treated as follows in a dark bottle :—

1. Immersed in 1·5 % silver nitrate at 37° C. (or five days at room temperature).
2. Washed in distilled water for several hours.
3. Reduced in 4 % pyrogallic acid, to which 5 % formalin has been added, for 24 hours at room temperature.
4. Washed thoroughly in distilled water.
5. Immersed in 80 % alcohol for 24 hours, in 95 % alcohol for 3 days, in absolute alcohol for 2 days, and, finally, treated with xylol, xylol-paraffin, and paraffin.

Particular stress is laid on the necessity for perfect fixation prior to treatment with silver, &c. Prolonged action of formalin gives the best results, interfering with the staining of neuroglia and accelerating that of *Sp. pallida*. Specimens which have rested in formalin for a year give the best results, though recent specimens have often been found suitable for examination. Sections are cut from 3–5μ in thickness, and the chances of finding the *Sp. pallida* seem to vary inversely with the intensity with which the neuroglia is stained. It is therefore best to commence the search in the palest part of the section. Noguchi recommends, in the cases of the spinal cord, that pieces 2 cm. long be cut and sections should be longitudinal.

Nakano (*Deutsche med. Wochenschr.*, November 9, 1912) recommends the following modification of Levaditi's stain :

1. The tissue is placed in formalin, 10 %, for 10–20 minutes.
2. Pieces 1–2 mm. thick are then put into alcohol, 95 %, for 3–5 hours.
3. Running water for 10 minutes.
4. Silver nitrate, 1·5 %, for 4–5 hours at 50° C. (in a black bottle).

5. A mixture of pyrogallic acid 3, formalin 10 % 5, distilled water 100, for 4–10 hours at 50° C.

6. Alcohol 95 % for 4–10 hours.

7. Absolute alcohol, xylol, paraffin.

Noguchi's Luetin Reaction. From time to time workers have experimented to discover, if possible, a method of diagnosing syphilis in a manner analogous to the cutaneous tuberculin reaction of von Pirquet, but till quite recently with doubtful success. Neisser produced a papular formation by inoculating the skin of syphilitics with extract of congenital syphilitic liver. A similar reaction was sometimes produced with normal liver extract. Meirowsky, Tedeschi, and Nicolas Favre and Gautier obtained similar reactions with extracts of syphilitic liver or of syphiloma, but Ciuffo failed with an extract of the organs of a congenital syphilitic. The results obtained by all these workers were inconclusive, probably because they were working too indirectly with the *Spirochaete pallida.*

In 1910–11 Noguchi made many experiments on rabbits with his cultures of *Spirochaete pallida.* Having prepared them with a series of intravenous injections of cultivated *Spirochaete pallida,* a month after the last injection he inoculated them intradermically with the same antigen and found that all of them had become allergic, the sites of inoculation becoming inflamed and sometimes pustular. Normal rabbits, on the other hand, did not react. Following on this he tried the emulsion of *Spirochaete pallida* culture on man, the emulsion being prepared from six strains of the micro-organism. The results showed that the reaction was strictly specific to syphilis, 250 persons who were normal or suffering from non-syphilitic diseases failing to react. This has been confirmed by Cohen, Robinson, and Kämmerer, who have published observations substantially in agreement with the following table, which shows Noguchi's results. Dr. Noguchi very kindly furnished me with a supply of luetin, and, with one exception mentioned below, my results have so far confirmed those of the above workers. Thirty-one patients suffering from other diseases were also tested and none of them gave the reaction. It will be noticed from Table IV that the luetin reaction is most positive in those cases of syphilis in which the Wassermann reaction is very likely to be negative, well-treated patients, and those in the later stages.

Preparation of Luetin. A pure culture of *Spirochaete pallida* in ascitic agar is rubbed up to a thick paste in a sterile mortar. To the thick paste which results is added little by little enough of a culture of *Spirochaete pallida* in ascitic fluid to make a perfectly liquid emulsion. This is sterilized by heating at 60° C. for an hour in a water-bath, and 0·5 per cent. tricresol added. In exactly the same way is prepared a control fluid made by rubbing up sterile culture-medium with liquid, heating and adding the preservative.

Method of Application. With a sterile pipette enough of each of the two fluids for the day's tests is diluted with an equal part of sterile normal saline. Using a separate syringe armed with a very fine needle, 0·07 c.c. of the diluted luetin is injected into the cutis vera of one upper arm and a similar quantity of the control in the same way into the other arm.

The Reactions. Negative. After twenty-four hours at each site of inoculation a small erythematous spot appears which recedes in forty-eight hours. No induration is left, but a small brownish papule about 3 mm. across may occasionally persist for some days.

Positive. Noguchi distinguishes three types :

(*A*) Papular. A large raised and indurated papule from 5–10 mm. in diameter appears in twenty-four to forty-eight hours. The indurated papule may be surrounded by a red area; the size and induration increase slowly for three or four days and then gradually subside. This reaction is given by secondary cases under regular treatment, and very young congenital syphilitics.

(*B*) Pustular form. Commences as a papule, but about the fourth day the surface becomes oedematous, and miliary vesicles may form. Within the next twenty-four hours a vesicle forms and this is succeeded by a pustule which soon ruptures, either spontaneously or on friction, and becomes covered with a crust. Soon after the rupture the induration subsides and practically

TABLE IV (Noguchi)

Luetin Reaction in Various Syphilitic Conditions and in Controls

	Primary Syphilis.		*Secondary Syphilis.*				*Tertiary Syphilis*				*Congenital Syphilis.*				*Cerebro-spinal Syphilis.*		*Latent Syphilis.*		*Controls.*			
	Symptoms Present.		*Symptoms Present.*		*Symptoms Absent.*		*Symptoms Present.*		*Symptoms Absent.*		*Under 1 Year.*		*Late Cases.*		*Symptoms Present.*				*Normal individuals.*		*Non-Syphilitic Cases.*	
Luetin reaction . .	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−	+	−
No antisyphilitic treatment	..	13	..	..	..	..	..	..	..	..	..	..	..	..	..	..	24	6	..	50	..	200
Slight mercurial treatment	1	12	2	25	..	..	12	..	..	..	5	18	..	..	..	..	..	..	..	..	..	..
Regular mercurial treatment . . .	..	..	..	..	14	3	31	..	29	1	1	3	15	1	5	5	..	..	..	..	..	..
Salvarsan and mercurial treatment . .	..	..	1	..	42	12	..	..	22	3	..	..	9	..	..	..	..	..	..	..	..	..
	1	25	3	25	56	15	43	0	51	4	6	21	24	1	5	5	24	6	0	50	0	200
	26		99				98				52				10		30		250			
	315																					

no scar is left. This type of reaction occurs most frequently in tertiary and late hereditary syphilis.

(*C*) Torpid form. This is rare. The immediate results of the inoculation appear to be nil, but after ten days or even longer the pustular form develops. This was observed by Noguchi in one case of hereditary syphilis, one of primary and two of secondary, all being under mercurial treatment. I have seen this form in one healthy person and am inclined to attribute it to late septic infection of the damaged area of skin.

The site of the control inoculation almost always becomes quite normal in appearance at the end of forty-eight hours, or at most a slight yellow pigmentation, the remains of an ecchymosis, may persist. Robinson noted in three cases which gave a severe luetin reaction of the pustular type a similar though smaller reaction at the control site. Two of these cases were tertiary and one was latent. In one of the cases I tested at Rochester Row an exactly similar result was obtained.

Though further investigation is necessary before the luetin reaction can be said to be strictly specific to syphilis, it will be seen from the table that a considerable amount of evidence has already accumulated in its favour. Since it is most often positive in the class of case which very frequently gives a negative Wassermann reaction, if its reliability becomes definitely established it will prove a valuable addition to our methods of diagnosis.

L W Harrison

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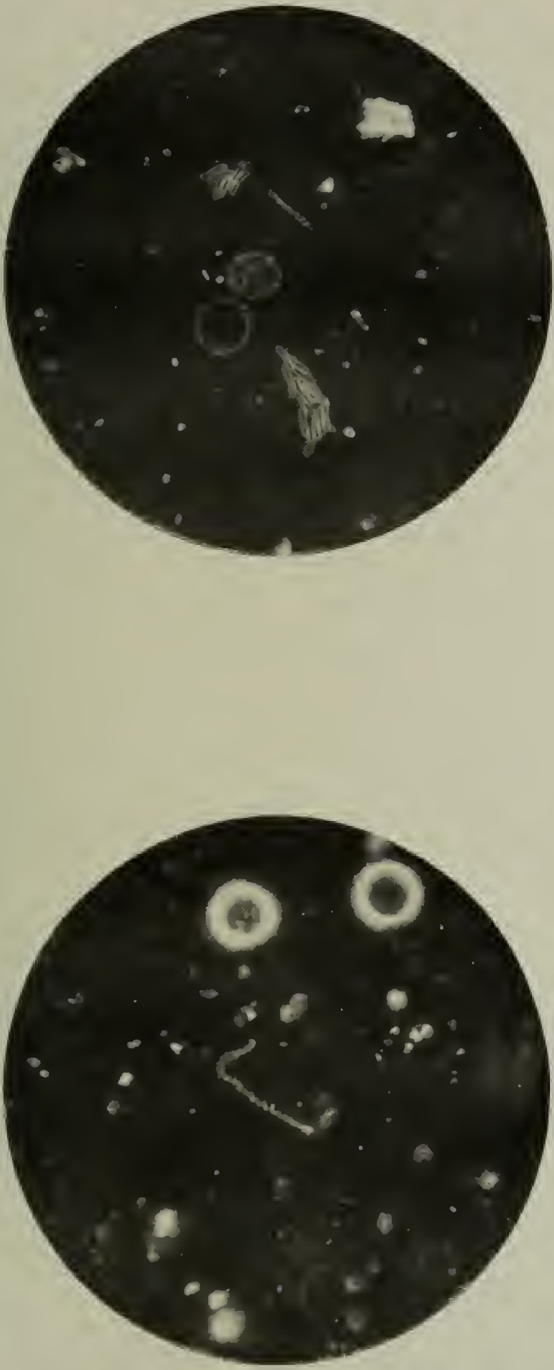

Plate LXIV.—Micro-photographs of living *Spirochaete pallida,* under dark-ground illumination with Leitz concentric condenser, magnified 850 diameters. Taken by Mr. Ogilvy.

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